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Bipolar Disorder in Pregnancy

Background

1. Definition
    - Bipolar disorder occurring in a pregnant pt
2. General information
    - Early dx and obstetric care is key to maximizing health of mother and fetus

Pathophysiology

1. See Bipolar Disorder
2. Lifetime incidence
    - Psychosis affects 1 in 600 pregnant women
3. Lifetime prevalence in women
    - Bipolar I: 0.9%
    - Bipolar II: 0.5%
4. Risk factors
    - Bipolar affective puerperal psychosis (severe postpartum psychosis), is clustered in families, linked to chromosome 16p13
5. Morbidity/ mortality
    - Premature delivery
        - Odds ratio: 1.40 vs normal controls
    - SGA infants
        - Odds ratio: 1.39 vs normal controls
    - Manic episode incr risk for alcohol/ drug consumption, incr risk to fetus
    - Lithium, valproate, carbamazepine teratogenic in first trimester (Class D)
    - Antidepressant use w/o concomitant anti-manic medication incr risk for mania and accelerated cycling
    - Manic/ depressive/ psychotic episodes follow 25-50% of deliveries
        - Highest risk in first pregnancy or pts w/prior severe postpartum relapses

Diagnostics

1. Diagnostic criteria
    - See Bipolar Disorder
2. Physical exam
    - Examine for medication SE (extrapyramidal symptoms)
        - Tardive dyskinesia
        - Resting tremor
        - Akinesia
        - Akathisia
        - Dystonia
        - "Lead pipe" rigidity
        - Postural instability
    - Mania S/S
        - Euphoria/ irritability
        - Decr need for sleep
        - Talkativeness
        - Racing thoughts
        - Hypersexuality

        - Aggression
        - Agitation
        - Poor judgment
    - Depression S/S
        - Insomnia/ early morning awakening
        - Decr interest
        - Guilt/ feelings of worthlessness
        - Fatigue
        - Poor concentration
        - Reduced appetite/ wt loss
        - Suicidal ideation
        - Hyposexuality
3. Diagnostic testing
    - Lithium level
        - Every 2-4 wks in pregnancy
        - Weekly in last month
        - Every 2-3 days before and after delivery
    - Check Thyroid function tests
        - 1-2 times during initial 6 mos of lithium tx
        - q6-12 mos in pts chronically tx w/lithium
        - When changes in S/S or side effects occur
4. Diagnostic imaging
    - High-resolution ultrasound at 16-18 wks to detect cardiac defects if treated w/lithium, valproate, or carbamazepine
5. Other studies
    - If treated w/lithium, valproate, or carbamazepine
        - Maternal serum AFP screen for neural tube defects before wk 20
        - Amniocentesis and sonography if elevated AFP

Differential Diagnosis

1. Major depressive disorder
2. Dysthymic disorder
3. Bipolar I disorder
4. Bipolar II disorder
5. Cyclothymic disorder
6. Bipolar disorder NOS
7. Post partum depression

Therapeutics

1. Acute tx
    - ECT indicated for pregnant pts w/severe mania or depression
        - May present less fetal risk than other medical tx
    - First generation high potency antipsychotics
        - ex: Haloperidol
    - Benzodiazepines
        - Lorazepam is preferred if necessary for tx of acute agitation

2. Further mgmt (24 hrs)
    - Pre-conception or 1st trimester
        - Taper off medication if mild/ moderate illness and avoid medication until at least second trimester
            - Close follow up is necessary to monitor for signs of relapse
    - Continue tx in pts that present for obstetric care in second or third trimester
    - High-potency first generation antipsychotic medications preferred especially in first trimester
        - Fluphenazine
        - Haloperidol
        - Perphenazine
        - Thiothixene
        - Trifluoperazine
3. Long-term care
    - Inform pt of high risk of postpartum relapse
    - Resume pre-pregnancy tx/ dose (lithium/ valproate) after delivery
    - Maintain normal sleep pattern postpartum to protect against manic episodes
4. Anti-manic agents
    - Lamotrigine
        - Pregnancy Category C
        - No documented incr in congenital anomalies
    - Typical antipsychotics
        - Pregnancy Category C
        - Not associated w/fetal anomalies
        - Haloperidol
        - Trifluoperazine
        - Perphenazine
        - Prochlorperazine
    - Atypical antipsychotics
        - Pregnancy Category C
        - Limited studies on teratogenicity
        - Monitor for wt gain, impaired glucose tolerance, and worsening lipid profile
        - Risperidone
        - Quetiapine
        - Olanzapine
        - Aripiprazole
    - Verapamil
        - Pregnancy Category C
        - Recommended for pts who respond to Lithium but cannot tolerate SE
        - Lack of teratogenicity supports use in pregnant bipolar pt
    - Lithium
        - Pregnancy Category D
        - Only mood stabilizer proven to reduce suicide in bipolar pts
        - Discontinue lithium during first trimester: weigh risks vs. benefits
        - Rate of relapse is incr by lithium discontinuation, especially if stopped abruptly

        - Absolute risk for Ebstein's anomaly:
            - 1-2 per 1,000 (10-20x risk in general population)
            - Apical displacement of posterior and septal tricuspid valve leaflets, atrialization of right ventricle, +/- ASD or patent foramen ovale
        - 3rd trimester use controversial:
            - Some studies show association with:
                - Hypothyroidism
                - Floppy baby syndrome
                - Premature delivery
        - Restriction in labor controversial
            - Restart when pt is medically stable postpartum, using preconception dose
            - Incr risk of lithium toxicity following delivery d/t large volume loss
        - Restriction in breastfeeding controversial
            - Recent study showed average breastfed infant serum lithium level = 0.16meq/L, and no adverse effects noted in infants
        - Therapeutic serum level: 0.8-1.2 meq/L
        - Toxicity at serum level ≥1.5 meq/L
            - Vertigo
            - Sedation
            - Arousal
            - Coarse hand tremor
            - Muscle weakness
            - Cardiac arrhythmias
        - Serum levels >2.5 meq/L
            - Coma
            - Renal failure
            - Seizures
            - Death
    - Valproate
        - Pregnancy Category D
        - Avoid during pregnancy
        - Spina bifida risk 1-5% (15-30 day post-fertilization)
        - Craniofacial and cardiac defects, polydactyly, hypospadias, low birthweight
        - SE: nausea, blurred vision, nystagmus, sedation, vertigo
        - Rarely: agranulocytosis, aplastic anemia
        - 4 mg Folic acid supplement recommended
    - Carbamazepine
        - Pregnancy Category D
        - Spina bifida risk 0.5-1.0% (15-30 day post-fertilization)
        - Meningomyelocele, anal atresia, ambiguous genitalia, cardiac defects, craniofacial abnormalities, torticollis
        - 4 mg folic acid supplement recommended
        - Additional 20 mg of vitamin K supplement daily at 36 wks until delivery

Follow-Up

1. Return to office if pt experiences:
   - Depression
   - Agitation
   - Manic symptoms
2. Time frame for return visit
   - Follow-up for eval of psychiatric status within first 2 wks postpartum
3. Refer to specialist
   - Women w/bipolar disorder should be referred to a psychiatric professional for eval and tx
   - Psychiatric consult ideal during hospitalization for delivery
4. Admit to hospital
   - Acute manic event/ relapse
   - Suicide/ homicide risk
     - Suicidal/ homicidal ideation/ intent/ plans
     - Access to means for suicide
     - Command hallucinations, other psychotic symptoms or severe anxiety
     - Alcohol or substance use
     - Hx of previous attempts
     - Family hx of or recent exposure to suicide

Prevention

1. Effective contraception for all female pts receiving drug tx for bipolar disorder
   - Carbamazepine, oxcarbazepine, and topiramate incr metabolism of OCPs
   - Do not rely on OCPs alone
2. Pregnancy should be planned in consultation w/psychiatrist

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