

Bipolar Disorder and Postpartum Psychosis

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Case

22y Haitian American G3P1021, with no past psych hx prior to recent postpartum episode, who was referred to the outpatient Perinatal Program s/p first lifetime hospitalization where she was treated for postpartum psychosis with down mood. Pt delivered a healthy baby girl via NSVD at 38.5 weeks, developed depressive sx the first week postpartum, with severe insomnia, which quickly developed into psychosis with delusions about the baby (the baby was giving her "the finger"), belief that her husband could read her mind, and AH telling her she was going to die, or was already dead, culminating in para-suicidal behavior of cutting her wrist in front of family "to make the voices stop." Pt was started on PO Risperdal while inpt, which was switched to Invega Sustenna, then augmented with Depakote (after brief and unsuccessful trial of Zolofte). She was also started on Depo Provera. Of note, pt's sister has Bipolar Disorder, and postpartum psychosis is often the first diagnosed episode of previously undiagnosed Bipolar Disorder. First break of primary psychotic disorder cannot be ruled out, however it is not the primary dx in the differential.

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What is Postpartum Psychosis?

Usually an affective psychosis (can be depressive, mixed state or have schizophrenia like features)
Usually appears early postpartum, typically within the first 4 weeks
Usually rapid onset
May have confusion and fluctuating course (can look like delirium)

PSYCHIATRIC EMERGENCY

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What to look for

Confusion/ **cognitive disorganization**
Strange beliefs (referential, persecutory, grandiose, about baby's identity)
Hallucinations (usually auditory, but can be any modality)
Disorganized behavior
"Appears more organic"

MAKE SURE TO ASK about thoughts to harm self and/or baby (can be ego syntonic in psychosis – as opposed to ego-dystonic in OCD)



Why is it an EMERGENCY?

Infanticide in approximately 4% of cases and "eventual suicide" in 5% of cases (Davidson 1985)

- This study sample was small (82 pts) who were ill in the late 1940s through early 1970s and diagnostic criteria were different, most actually dx unipolar depression (52%), followed by bipolar (18%) followed by schizophrenia (16%), abnormal personality with depression (8%), and organic disorder (2%)
- Suspect this is overestimate, however heightened risk is real



Complications

Increased risk of infanticide
Increased risk of suicide

- risk of completed **suicide 2 out of 1,000 women with postpartum psychosis (newer estimate)**
- means of death more likely to be irreversible (jumping from heights) than non-violent means (overdose)

delayed social, emotional and cognitive development in infant



Epidemiology

About 1-2/ 1000 births (incidence of hospitalization for psychosis in 90 days postpartum)

Risk rises to 1/ 7 for women with h/o previous postpartum psychosis

Compare to risk for postpartum depression - approx 15% general population



Risk Factors and Differential Diagnosis



Isolated Postpartum Psychosis

For some women, risk of psychosis or mania is limited to the postpartum period

Likely represent a unique diagnostic entity

Important to remember that while Bipolar Disorder is a MAJOR risk factor for PP, not every case of PP is Bipolar D/O

These women do not appear at increased risk at other (non puerperal) times, including DURING pregnancy, and therefore are generally not prophylaxed until after childbirth when they are at INCREASED risk of recurrence.



Bipolar Disorder as a Risk Factor for Postpartum Psychosis

Association between Bipolar Disorder and Postpartum Psychosis
studies that look at women with h/o Bipolar
longitudinal studies of women with puerperal episodes of psychosis
family studies

All support a link between Bipolar Disorder and Postpartum Psychosis



Bipolar Disorder as a Risk Factor for Postpartum Psychosis

BIPOLAR DISORDER

- 74% of mothers with bipolar disorder and first-degree relative with postpartum psychosis
- 30% of mothers with bipolar disorder and no family history of postpartum psychosis (J and C 2001)
- women who stop mood stabilizer (esp lithium) more likely to experience recurrence of postpartum psychosis compared to those who remain on antimanic treatment (70% vs 24%) (Viguera 2000)
- history of postpartum psychosis in women with bipolar disorder or schizoaffective disorder associated with > 50% risk for recurrent postpartum psychosis



Risk Factors continued

Previous Postpartum Psychosis (without episodes outside perinatal period)
Risk of PP 29%

Bipolar Disorder
Risk of PP 17%

Both
not enough data, but higher



Differential Dx

Secondary Psychosis (ie psychosis due to)

- Substance Induced (especially "K2" in our hospital)
- Medical causes
 - Delirium/ infection
 - Stroke
 - Thyroid dysfunction
 - Encephalopathy (autoimmune encephalitis with anti NMDA receptor auto-antibodies, eclampsia related, PRES)

Postpartum Depression (with psychosis)
OCD (with obsessions reaching delusional severity)

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Prognosis



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Prognosis

good prognosis WITH TREATMENT, especially when symptoms arise < 1 month post-delivery

Compared with *non postpartum new onset* psychosis, women with postpartum onset (before 4-6 weeks post delivery) had:

- higher levels of confusion and disorientation
- required LESS time to achieve response

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Prognostic Factors

predictors of recurrence

- personal history
- family history
- BIPOLAR DISORDER
- cessation of antimanic treatment



Treatment





Treatment of Bipolar Disorder Perinatally

CONFIRM ACCURATE DIAGNOSIS

- Consider the possibility Bipolar Disorder may be over-diagnosed in pt's with BDPD
- Also consider Bipolar Disorder may be under-diagnosed in pt's with "h/o unipolar depression"

Examine pt's personal treatment history (med trials, periods off meds, number of occurrences, severity, risk) and document carefully

Most discussions (including parts of this lecture) tend to focus more on SAFETY than EFFICACY. Efficacy is PARAMOUNT. Inadequately treating is the worst of both worlds.



When discussing risks of treatments

Compare risks of treatment with risks of illness

Discuss and document comorbid factors that may influence risk (BMI, GMC, lifestyle habits, etc)

Don't forget risks in general population

- Baseline risk of malformations in general population is about 2-4%



Medications

Will discuss meds used for tx of Bipolar, but many are not common anymore since rise of SGAs

Usually end up considering

- SGAs
- lithium
- lamictal
- benzos



Valproic Acid

AVOID!!!!!!!!!!!!!!!!!!!!!!!!!!!!!!!!!!!!

50-100x more teratogenic than lithium

1st trimester exposure

- 5% risk of neural tube defects
- 2-7x increased risk of ASD, hypospadias, cleft palate, polydactyly, craniosynostosis
- 12-16x increased risk for spina bifida



Valproic Acid

Can you restart after first trimester?
NOT RECOMMENDED!

- Neurocognitive delays, increased risk for autism, lower IQ- have all not been defined through trimester specific exposure
- Decreases vitamin K (increased risk of bleeding)



What if you “have to?”

Lowest effective dose (malformation risk is correlated with blood level)
PNV
FA (4-5mg per day!)

- Not clear it actually lowers risk of neural tube defects, but did reduce risk of miscarriage

Vitamin K (20mg per day_ during last month of pregnancy)

- To avoid bleeding problems in mother and newborn



Valproic Acid- lactation

Could be done carefully
Need to monitor levels in infant

- VPA level
- Platelets
- LFTs

Even low levels may contribute to hepatotoxicity



Carbamazepine

Not used much anymore, monitor levels
MCM 3.3% (slightly higher than baseline)
Spina bifida only birth defect significantly associated
PNV, FA, vit K (similar to VPA)
Breastfeeding
• Most infants do fine
• 3 cases of hepatic dysfunction
• Monitor drug level, LFTs, CBC in infant



Oxcarbamazepine (Trileptal)

Limited data
Rec: PNV, FA
Follow levels
2.8% risk of MCM
Breastfeeding- limited data but no adverse events reported



Topiramate

Limited data
Rec: PNV, FA
Follow levels
5% risk of MCM and 5.1% risk hypospadias
2.2% risk oral clefts
Breastfeeding- thought to be safe, limited data



Gabapentin

Possibly better option for those in whom it has been EFFECTIVE
Rec: PNV, FA
Limited data, may want to follow levels
1.7% risk MCM (within baseline)
Breastfeeding- limited data, but no adverse events reported



Lamotrigine

Promising for pregnancy and lactation
Requires little monitoring
Overall risk of birth defects within baseline population range
Recommend PNV and FA



Lamotrigine- risk for Cleft Palate?

2006 FDA issued warning about risk of cleft palate

- Based on one study estimated risk as 8.9/1,000 (vs baseline 0.5-2.16/1,000)
- Later studies found risk of 0.7% and 0.25%, or no increased risk at all



Lamotrigine and Estrogen

Estrogen decreases lamotrigine levels by as much as 50% (estrogen induces metabolism by conjugation)
Dose may need to be increased during pregnancy, and decreased postpartum
Clinical monitoring considered sufficient, but most take levels to follow



Lamotrigine- lactation

M/P ratio is higher than with many other medications
Thought to be safe
Most studies showed no adverse events
Only one case report of 16 day old infant with apnea

- Mother was taking 850mg per day



Treatment - Lithium

Yes we CAN and WE likely SHOULD MORE
We don't we?

- People are afraid of Epstein's Anomaly
- Requires careful dosing ante and postpartum
- Breastfeeding not recommended



Lithium- why SHOULD we?

For pregnant women with bipolar disorder and stabilized on medication

- continuing lithium in pregnancy helps to reduce relapse (Viguera et al 2000; Viguera et al 2007a).

For women who discontinue lithium during pregnancy

- lithium immediately after the birth to reduce recurrence (Cohen et al 1995; Wisner et al 2004)



Lithium- Epstein's Anomaly

Congenital defect of tricuspid valve (valve between R chambers)
Causes back leak, less efficient blood pumping, risk of heart failure
Tx may involve just monitoring, medications or valve repair
Baseline risk in general population 1/ 20,000
Risk with 1st trimester exposure to lithium 1/ 1-2,000
Large relative risk but low absolute risk



Lithium- Dosing considerations

Crosses placenta easily

- so use lowest effective dose
- BID dosing

Sensitive to hydration and fluid shifts

- May need to increase dose during pregnancy and decrease postpartum
- Stop lithium few days prior to delivery
- Restart postpartum at half dose and check levels



Lithium - monitoring

Level II ultrasound and fetal echo at 18-20 weeks
Check lithium level, BUN, Cr and electrolytes MONTHLY
Check TSH mid pregnancy



Lithium and Lactation

Breastfeeding **CONTROVERSIAL**
Used to be contraindicated by AAP, now with warning
Easily excreted into milk (it's a salt) with a narrow therapeutic index
If necessary, check infant lithium level, BUN, TSH, electrolytes and Cr immediately postpartum, at 4-6w, then Q 8-12w



Benzodiazepines

Animal study (400X equiv human daily dose) showed inc risk cleft lip and palate
Early human case control also showed very small (0.7%) increased risk
Later studies and pooled data does not support this association
Some reports of "floppy baby" and neonatal withdrawal on higher doses



Benzos and lactation

At usual lower doses, relatively safe
Levels rise and fall in breast milk at same rates as in serum
Prefer shorter half life and no active metabolites

- (ie Ativan)



First Generation Antipsychotics

Do not appear to be associated with MCM
Can be assoc with neonatal "withdrawal" and EPS
Can last up to several months (but usually few weeks)
Most data appears for Haldol due to how old medication is and frequency of use over decades
Not as much data for mood stabilization so probably not as good a choice, unless h/o good response



Second Generation Antipsychotics

Previous studies indicated SGA associated with increased risk for GDM, whereas FGA was not
Previous studies- inconsistent

- Increased birth weight / LGA
- Decreased birth weight/ SGA
- No difference



Quetiapine (Seroquel)

Lower rates of placental transfer as compared with risperidone and olanzapine
Suspected only small changes in maternal serum levels during pregnancy
No increased risk of fetal malformations or adverse neonatal outcomes in prospective studies
Delays in ossification were seen in rats and rabbits at doses comparable to human range
Reasonable FIRST CHOICE when new atypical is indicated for pregnant pt



Olanzapine (Zyprexa)

Anecdotal post-marketing cases of fetal malformations but several larger studies did not find higher rates of MCM or any pattern
Animal data show no teratogenicity
Higher placental passage as compared with quetiapine or risperidone
Neonatal withdrawal syndrome described
Possibly higher rates of GDM and associated complications
Good choice in woman with h/o positive response



Risperidone (Risperdal)

Rates of placental passage higher than Seroquel
No major teratogenic effects
Possible withdrawal emergent syndrome in neonate (tremors, irritability, poor feeding, somnolence) but not associated with other adverse events
POINT- due to tendency to cause hyperprolactinemia, may decrease fertility and make it more difficult to maintain early pregnancy
Not great choice for women wanting to conceive or early in pregnancy



Lurasidone (Latuda) (B)

Very limited data in humans (newer drug)
Animal data show no evidence of teratogenicity or embryo-fetal toxicity in rat and rabbit studies up to 12x max rec human dose



Ziprasidone (Geodon)

Little data
Manufacturer data
• 5 spont ab, 1 stillbirth, 1 malformation among 57 exposures
Animal data suggest developmental toxicity and impaired fertility
Too little data to draw good conclusions, but not first choice compared with other SGAs



Iloperidone (Fanapt)

Very little data in humans
Animal studies suggested increased intrauterine deaths, decreased fetal weight and length, decreased skeletal ossification
Similar to Geodon, not enough human data but not preferred



Paliperidone (Invega)

Also limited human data, but slightly more than Geodon and Fanapt
Should theoretically overlap with Risperdal profile to a large degree
Animal studies- no increase in fetal abnormalities
Appears good for breastfeeding – limited data show low or undetectable infant serum levels (consider for postpartum psychosis in breast feeding mother)



Aripiprazole (Abilify)

Animal studies suggest teratogenic potential at 3-10 x equivalent max human daily dose
Fewer human studies than other SGAs
Placental transfer on lower end (cord to maternal serum concentration ratios of 0.47-0.63)
Good choice for woman with h/o good response, but not first choice in tx naïve cases



Clozapine (B)

No increased teratogenicity at 2-4 x max human daily dose
Increased risk for GDM and associated macrocephaly
Agranulocytosis and severe constipation as well as other side effects as seen in non-pregnant population, also make this medication non first line choice, however in pt with h/o response, or NEEDING clozapine, would not discontinue it

NOT COMPATIBLE WITH BREASTFEEDING



Treatment of Postpartum Psychosis (new onset illness)

Same as treating psychosis at any other time, but keeping in mind

- Probably Bipolar Disorder (so do not do anything that would worsen Bipolar Disorder)
- Breastfeeding preferences and profiles
- Future family planning

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What About that Algorithm?

FIRST onset psychosis in PP period

Step 1 – benzos QHS x 3 days
Step 2 – ADD antipsychotics x 2 weeks
Step 3 – ADD lithium x 12 weeks
Step 4 – ECT

98.4% achieved remission within first 3 steps (none needed ECT)
At 9mo, those treated with lithium had lower rates of relapse compared with antipsychotic

Conclusion: structured algorithm leads to high remission rates, and maintenance with lithium leads to better relapse prevention

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ECT

Safety during pregnancy well documented in last 50 years
Well documented guidelines and changes for pregnancy – well studied
Risks= usual ECT risks (STM, anesthesia, etc)
Most common risk to fetus- fetal bradyarrhythmias (2.7% of cases) led to recommendation for pre-oxygenation and elevate R hip to decrease aorto-caval compression
Most common risk to mother- premature contractions (3.5% of cases) led to recommendation to choose beta2 adrenergic tocolytics (to suppress labor)

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Bottom Line

Stay away from Depakote!

Consider what is EFFECTIVE for that particular patient

Usually choosing between SGA, lithium, lamictal, plus or minus benzos

Of the atypicals, all other things being equal, more data supporting quetiapine, olanzapine and risperdone (but not risperdone as favored for pre-conception or early pregnancy)



Thank You!

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References

Bergink, V., Boyce, P., & Munk-Olsen, T. (2015). Postpartum psychosis: a valuable misnomer. *Australian and New Zealand Journal of Psychiatry*, 49(2), 102-103.

Chaudron, L. H., & Pies, R. W. (1899). The relationship between postpartum psychosis and bipolar disorder: a review. *The Journal of clinical psychiatry*, 64(11), 1284-1292.

Davidson, J., & Robertson, E. (1985). A follow-up study of post partum illness, 1946-1978. *Acta Psychiatrica Scandinavica*, 71(5), 451-457.

Dynamed

Jones, Ian, and Nick Craddock. "Familiality of the puerperal trigger in bipolar disorder: results of a family study." *American Journal of Psychiatry* (2001).

Epperson CN. Postpartum major depression: detection and treatment. *Am Fam Physician* 1999 Apr 15;59(8):2247-54, 2259-60

Harlow, B. L., Vitonis, A. F., Sparen, P., Cnattingius, S., Joffe, H., & Hultman, C. M. (2007). Incidence of hospitalization for postpartum psychotic and bipolar episodes in women with and without prior prepregnancy or prenatal psychiatric hospitalizations. *Archives of General Psychiatry*, 64(1), 42-48.



References

Heron, J., Gilbert, N., Dolman, C., Shah, S., Beare, I., Dearden, S., ... & Ives, J. (2012). Information and support needs during recovery from postpartum psychosis. *Archives of women's mental health, 15*(3), 155-165.
PLOS Med 2009 Feb 10;6(2):e13
Sit, Dorothy, Anthony J. Rothschild, and Katherine L. Wisner. "A review of postpartum psychosis." *Journal of women's health 15.4* (2006): 352-368.
Scottish Intercollegiate Guidelines Network (SIGN) national clinical guideline on management of perinatal mood disorders. SIGN 2012 Mar
Spinelli MG. Postpartum psychosis: detection of risk and management. *Am J Psychiatry.* 2009 Apr;166(4):405-8
Spodniaková, B., Halmo, M., & Nosáľová, P. (2015). Electroconvulsive therapy in pregnancy-A review. *Journal of Obstetrics and Gynaecology, 35*(7), 659-662.



References

Viguera, Adele C., et al. "Risk of recurrence in women with bipolar disorder during pregnancy: prospective study of mood stabilizer discontinuation." *American Journal of Psychiatry* (2007).
Viguera, Adele C., et al. "Managing bipolar disorder during pregnancy: weighing the risks and benefits." *Canadian Journal of Psychiatry 47.5* (2002): 426-436.
Vigod, S. N., Gomes, T., Wilton, A. S., Taylor, V. H., & Ray, J. G. (2015). Antipsychotic drug use in pregnancy: high dimensional, propensity matched, population based cohort study. *bmj, 350*, h2298.
Wisner, K. L., Peindl, K., & Hanusa, B. H. (1994). Symptomatology of affective and psychotic illnesses related to childbearing. *Journal of Affective Disorders, 30*(2), 77-87.
Wesseloo, Richard, et al. "Risk of postpartum relapse in bipolar disorder and postpartum psychosis: a systematic review and meta-analysis." *American Journal of Psychiatry* (2015)
Yonkers, K. A., Vigod, S., & Ross, L. E. (2012). Diagnosis, pathophysiology, and management of mood disorders in pregnant and postpartum women. *FOCUS*.


