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Psychiatry and Addictions Case Conference

UW Medicine | Psychiatry and Behavioral Sciences

MANAGING BIPOLAR DISORDER IN PREGNANCY

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project ECHO

GENERAL DISCLOSURES

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SPEAKER DISCLOSURES

No conflicts of interest

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OBJECTIVES

1. Describe the prevalence of perinatal bipolar disorder and risk of recurrence
2. Summarize treatments for bipolar disorder during pregnancy and postpartum
3. Apply knowledge of risks of untreated bipolar disorder and risks of medications to informed consent discussion

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CASE

- 25 yo female with h/o Bipolar Disorder I, maintained stable mood on lithium for 4 years. Had 1 episode of mania 5 years ago and 1 episode of severe depression 4 years ago. She presents for pre conception counselling.

BIPOLAR DISORDER IN PREGNANCY

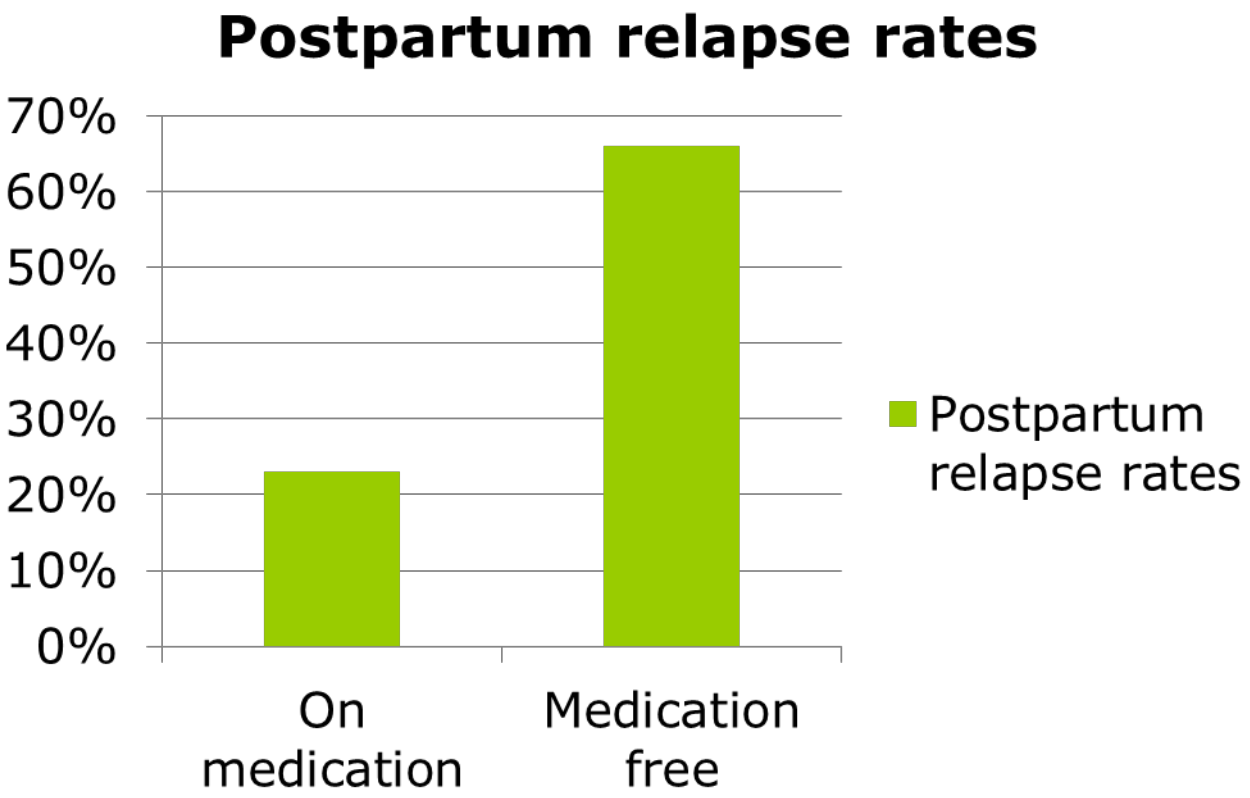
- Women with BD who discontinue their medication before or during pregnancy have a 60 - 70% risk of recurrence (most frequently in 1st trimester)
- Stopping medications during pregnancy also increased the risk for PP episodes (66% compared to 23%)
- Higher risk of antepartum hemorrhage, placental abnormalities and C section

Viguera et al 2007; Jablensky 2005

BIPOLAR DISORDER IN THE POSTPARTUM PERIOD

- Women with BD
  - 50% more likely to have PPD than women with MDD
  - 7 times more likely to be hospitalized for a first time mood episode
  - have a 25 to 50% increase risk for PP

RISK OF POSTPARTUM RELAPSE



(Wesseloo et al., 2015, American Journal of Psychiatry)

PREDICTORS OF POSTPARTUM RELAPSE

- Number of recent admissions
- Recent self harm
- Smoking
- Non white ethnicity
- Not on regular medication in first trimester
- Previous perinatal history of affective psychosis OR depression

Taylor et al, 2018; Di Florio et al 2018

EFFECTS OF THE DISEASE; EFFECTS OF THE TREATMENT

Bipolar Disorder

Anti-psychotics; Mood Stabilizers

- Poor prenatal and self care, subs abuse, fetal abuse or neonaticide
- Prematurity, microcephaly, neonatal hypoglycemia
- Longer term effects due to poor bonding

- GDM, higher rates of CS
- LBW, preterm
- Teratogenicity
- Neonatal syndromes
- Long term neurocognitive outcomes

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PHARMACOTHERAPY OF BIPOLAR DISORDER

- Mood Stabilizers:

  Lithium
  Valproate (Depakote)
  Carbamazepine (Tegretol)
  Oxcarbazepine (Trileptal)
  Lamotrigine (Lamictal)

- Antipsychotics

  SGAs : olanzapine, quetiapine, aripiprazole, risperidone, paliperidone, lurasidone

  FGAs: haloperidol, perphenazine

- Benzodiazepines

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LITHIUM AND MALFORMATIONS

- ?Increased risk of Ebstein's anomaly
- No significant difference in major cardiac malformations (2.1% (0.5%-3.7%) vs 1.6% (1.0%-2.1%).
- Most robust data on prophylactic benefit of mood stabilizer during the peripartum period are with lithium.

Patorno, 2017; Munk Olson 2018

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LITHIUM AND PREGNANCY OUTCOMES

- Main outcome measures: pregnancy complications, delivery outcomes, neonatal readmission to hospital within 28 days of birth
- Lithium exposure was not associated with any of the predefined pregnancy complications or delivery outcomes.
- Increased risk for neonatal readmission within 28 days of birth for lithium (pooled prevalence 27·5% [95% CI 15·8-39·1] vs 14·3% [10·4-18·2])

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PRESCRIBING LITHIUM IN PREGNANCY

- If possible, reduce dose in first trimester
- Considerations with hyperemesis
- Twice daily dosing to minimize peak levels/ side effects
- Blood level monitoring – monthly upto 34 weeks; weekly thereafter
- Fetal anomaly US (fetal cardiac scanning) at 16 – 20 weeks GA

Wesseloo 2017

LITHIUM AND DELIVERY

- Higher lithium levels at delivery associated with:
  - Lower Apgar scores
  - Longer hospital stays
  - More CNS, neuromuscular complications
- Lithium level when patient presents for delivery and 24 hours after delivery
- Adequate hydration; Considerations for pain relief
- Cord blood Li, TSH, Free T4
- Pre-conception dose once medically stabilized

Newport et al., Am J Psychiatry, 2005; Deligiannidis 2017; Poels et al 2018

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LITHIUM USE POSTPARTUM

- Consider a higher target therapeutic lithium level for the 1st PP month (0.8-1mmol/L)
- Twice weekly lithium blood levels in 1st 2 PP weeks
- Breastfeeding generally not recommended

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LITHIUM

Most data on prophylaxis, treatment and recurrence rates after discontinuation

Long term data reassuring

No effects on intrauterine growth

May need additional antipsychotics

Breastfeeding

First trimester exposure - Ebstein's anomaly -0.01–0.05% compared to a population risk of 0.005%

Frequent monitoring

Diav Citrin et al Am J Psychiatry 2104

LAMOTRIGINE IN PREGNANCY

- Not inferior to lithium in the prevention of severe PP episodes
- Prospective study from teratology service (median dose 200 mg/d): No increase in MCM. No cases of oral cleft
- 29% needed dose increase during pregnancy (2 -3 times)
- Ideally check pre pregnancy euthymic level
- Monthly monitoring of levels
- No neurodevelopmental disorders in children exposed to in utero lamotrigine (up to 6 years)

Diav Citrin 2017; Dolk 2016 ; Pariente 2017

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LAMOTRIGINE IN THE POSTPARTUM PERIOD

- If dose was increased during pregnancy, taper to pre pregnancy dose within 2 weeks:
  - decrease by 25% immediately PP
  - decreased every 3 -4 days until prepregnancy dose is reached

- If breastfeeding, infant doses are 6% to 50%; no contraindication to breastfeeding

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SECOND GENERATION ANTIPSYCHOTICS AND MALFORMATIONS

- No increased risk:

  Aripiprazole, Olanzapine, Quetiapine
- Minor increased risk:

  Risperidone, Paliperidone (RR 1.26)
- Insufficient data:

  Amisulpiride, Asenapine, Lurasidone, Sertindole

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SECOND GENERATION ANTIPSYCHOTICS AND PREGNANCY / NEONATAL OUTCOMES

- No increased risk:
  Miscarriage
  Stillbirth
  SGA
- ?Possible increased risk of GDM and LGA
- No delays in cognitive motor or social emotional development at 6 and 12 months
- Not possible to stratify on individual drug level

Damkier et al 2018; Clark et al 2018

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MOOD STABILIZERS: CONGENITAL MALFORMATIONS

Valproate	< 700 mg/d	5.6%
	700-≤ 1500	10.4%
	≥1500 mg/d	24.2%
Carbamazepine	< 400 mg/d	3.4%
	400-≤ 1000	5.3%
	≥ 1000 mg/d	8.7%
Lamotrigine	< 300 mg/d	2.0%
	≥ 300 mg/d	4.5%

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MOOD STABILIZERS: NEURODEVELOPMENTAL OUTCOMES

Mood Stabilizer	Number of Studies	Findings
Antiepileptics	10	Poor global cognitive abilities; dose response for valproate
Lithium	2	No adverse neurodevelopmental outcomes
SGA	3	Early delay, resolved by 12 months

Haskey et al, 2017

BENZODIAZEPINES

- Teratogenicity - ± oral clefts, cardiac malformations
- Chlordiazepoxide and diazepam – safest; some data for clonazepam.
- Use in third trimester – floppy baby, hypothermia, respiratory suppression, withdrawal
- Long term – lower developmental quotient at 10 and 18 months
- Use liberally in postpartum period to ensure sleep and prevent postpartum psychosis

BABY NEEDS ATTENTION TOO

- In utero antipsychotic exposure – feeding disorder, hypotonia, hypertonia, tremor, agitation, somnolence, respiratory distress
- In utero exposure to Lithium: monitor renal and thyroid function
- Breast milk exposure – Monitor for side effects

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ANTIPSYCHOTICS AND LACTATION

Medication	Relative infant dose	Adverse effects	Compatibility
Haloperidol	0.2 – 9.6	Delayed psychomotor development	+
Chlorpromazine	0.1 – 0.2	Delayed psychomotor development Sedation Lethargy	+
Risperidone	2.8-4.7	-	±
Olanzapine	<0.1-4	-	+
Aripiprazole	0.8	-	+
Quetiapine	0.1-0.5	Sedation	+
Ziprasidone	1.2	?	?
Clozapine	1.0-1.1	Agranulocytosis, seizures	-

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MOOD STABILIZERS AND LACTATION

Medication	Relative infant dose	Adverse effects	Compatibility
Lithium	3.1- 69	hypotonia, lethargy, hypothermia, inversion of ECG wave	-
Valproate	0.1 – 3.9	Thrombocytopenic purpura, anemia, and reticulocytosis	+
CBZ	1.1-7.3	poor suckle, poor weight gain, sedation, transient hepatic dysfunction	+
Lamotrigine	1.8-21.1	Sedation, respiratory suppression	+

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NON MEDICATION INTERVENTIONS

- Psychoeducation
- Sleep
- Post discharge IOP
- Parenting support
- IPSRT, MBCT
- In home services

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LIGHT THERAPY

- Bipolar Depression: Midday, 7000 lux, titrate up from 15 min to 60 min in 4 weeks, for 6 weeks

Clark et al, 2018

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CASE

- 25 yo female with h/o Bipolar Disorder I, maintained stable mood on lithium for 4 years. Had 1 episode of mania 5 years ago and 1 episode of severe depression 4 years ago. She presents for pre conception counselling.

KEY QUESTIONS

- Diagnostic clarification
- Preconception counseling: timeline
- Prior medications, prior periods off medication
- If already pregnant, gestational age?
- Risk factors for relapse

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FURTHER READING

- Clark, C. T., & Wisner, K. L. (2018). Treatment of Peripartum bipolar disorder. *Obstetrics and Gynecology Clinics*, *45*(3), 403-417.

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RESOURCES

- https://mothertobaby.org/
- Lactmed: https://toxnet.nlm.nih.gov/newtoxnet/lactmed.htm
- MGH Center for Women's Mental Health: https://womensmentalhealth.org/
- UW Perinatal Psychiatry Consultation Line

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PERINATAL PSYCHIATRY CONSULTATION LINE / PAL FOR MOMS

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Partnership Access Line (PAL) for Moms

Formerly Perinatal Psychiatry Consultation Line

Providing telephone consultation to healthcare providers caring for women with mental health needs during pregnancy and postpartum

206-685-2924 or
877-725-4666 (PAL4MOM)

Weekdays from 1-5 PM

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MOM'S ACCESS PROJECT

Help us help women get the
perinatal mental health care they need!

Are you in a profession that cares for pregnant and new moms? Please take our brief survey to help us identify all providers in Washington State who care for women with perinatal mental health or substance use problems. With this information, we hope to help primary care and obstetric care providers connect every woman in need of perinatal mental health support with a provider.

To take the survey:
Scan the QR code to the right with your phone or visit https://is.gd/momsaccessproject

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