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Psychiatry and Addictions Case Conference

UW Medicine | Psychiatry and Behavioral Sciences

MOOD STABILIZERS IN PREGNANCY

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Integrated Care Training Program
UW Psychiatry & Behavioral Sciences

project ECHO

GENERAL DISCLOSURES

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GENERAL DISCLOSURES

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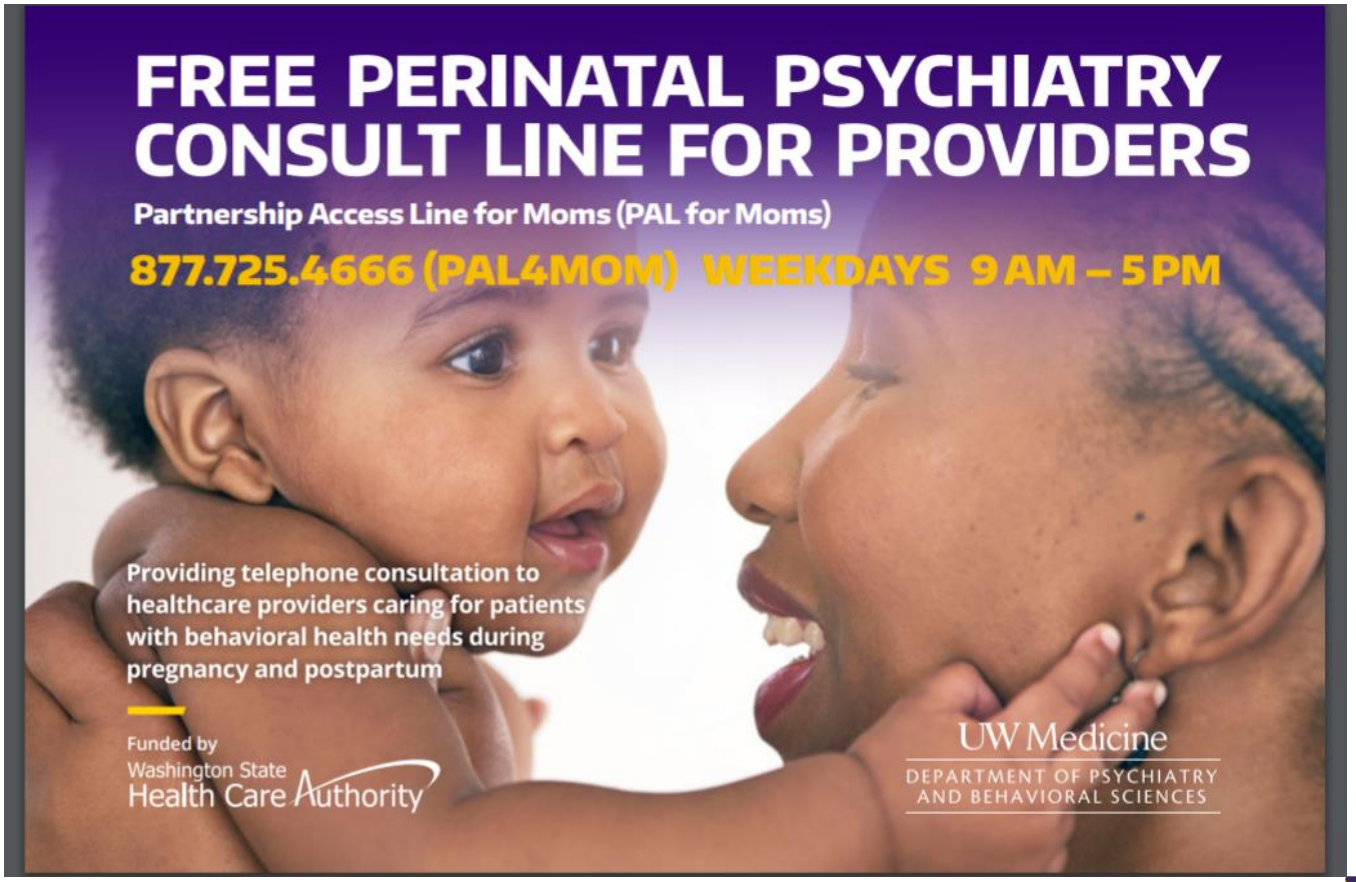
SPEAKER DISCLOSURES

- ✓ PAL4MOMS



PLANNER DISCLOSURES

The following series planners have no relevant conflicts of interest to disclose:

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OBJECTIVES

1. Summarize reproductive safety information for mood stabilizers
2. Understand recommended medication management approaches for bipolar disorder in pregnancy
3. Apply knowledge of risks of untreated bipolar disorder and risks of medications to informed consent discussion

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CASE

- 35 yo married female G1 at 16 weeks gestation presents with depression, PHQ-9 of 12, no suicidal ideation. She has had 1 depressive episode in the past. She tells you she did not tolerate sertraline or citalopram. When asking for more details on her response to sertraline and citalopram she tells you she became very agitated, felt like she was on speed, and stayed up all night for 4 nights, cleaning the house. What would you recommend?

A. Lamotrigine
B. Lithium
C. Venlafaxine
D. Watchful waiting

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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 neurodevelopmental disorders in children exposed to in utero lamotrigine (up to 6 years)
- 29% need dose increase during pregnancy (2 -3 times)
- Check pre pregnancy euthymic level; monitor monthly

Diav Citrin 2017; Dolk 2016 ; Pariente 2017

LAMOTRIGINE IN THE POSTPARTUM PERIOD

- If dose was increased during pregnancy, taper to pre pregnancy dose within 2 weeks:
  - decrease by 25% immediately PP
  - decrease 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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CASE

- 25 yo female with diagnosis of bipolar disorder type 1 , onset at age 14, 5 hospitalizations for mania or severe depression with suicidal ideation, stable on 1200 mg lithium for the past year. She wants to get pregnant in the next 6 months. What would you recommend?

A. Cross taper to lamotrigine
B. Continue lithium
C. Stay off lithium for the first trimester
D. Postpone thinking about pregnancy

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LITHIUM: CONGENITAL MALFORMATIONS

- ? Ebstein's anomaly
  - Baseline 1 in 20,000; Lithium 1 in 1000
- Risk for cardiac malformations: adj RR of 1.65 (95% CI, 1.02-2.68)
- No significant difference in major cardiac malformations (2.1% (0.5%-3.7%) vs 1.6% (1.0%-2.1%).
- Major malformations higher than the general population (7.4% vs 4.3%)

Patorno 2017; Munk Olson 2018

LITHIUM AND PREGNANCY OUTCOMES

- Increased risk of miscarriage?
- Not associated with any 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])

Poehls et al, 2020

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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

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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CASE

- 35 yo married female G1 at 6 weeks gestation presents with severe depression, PHQ-9 of 21, no suicidal ideation. She has had 5 depressive episodes in the past, one leading to psychiatric hospitalization for suicidal ideation, and 2 episodes of hypomania. What would you recommend?

A. Lamotrigine
B. Lithium
C. Venlafaxine
D. Quetiapine

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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 of:
  - Miscarriage
  - Stillbirth
  - SGA
- GDM more common in women taking quetiapine (RR=1.28, 95% CI=1.01-1.62) and olanzapine (RR=1.61; 95% CI=1.13-2.29)
- Neonates - feeding difficulty, hypotonia, hypertonia, tremor, agitation, somnolence, respiratory distress
- No delays in cognitive motor or social emotional development at 6 and 12 months
- Not possible to stratify on individual drug level
- Most are compatible with breastfeeding

Damkier et al 2018; Clark et al 2018

NON MEDICATION INTERVENTIONS

- **Sleep**
- Light therapy
- Post discharge IOP
- Parenting support
- IPSRT
- In home services

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RULES OF THUMB IN PRESCRIBING FOR PERINATAL MENTAL HEALTH DISORDERS

- Changes to meds to be made before pregnancy if possible
- Ideally patient should be psychiatrically stable for at least three months before attempting to conceive
- Use medications with more safety information
- Minimize number of exposures
- Use a team approach
- Be supportive if the patient goes against your recommendations
- Recommend folic acid prenatally
- Don’t forget non – medication factors!

Chisolm et al 2016

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KEY QUESTIONS

- Diagnostic clarification
- Treatment preferences
- Preconception counseling: timeline
- Prior medications, prior periods off medication
- If already pregnant, gestational age?
- Severity of illness
- Access to psychotherapy and social support

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ASSESSING SEVERITY OF ILLNESS

- Age of onset
- Multiple episodes (> 3 or 4)
- Recovery between episodes
- Abrupt onset of symptoms
- Psychotic mania / severe depression
- Hospitalization / suicidal ideation
- Past peripartum episodes
- Comorbidity

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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 (PPP)
- 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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RESOURCES

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

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PERINATAL PSYCHIATRY CONSULTATION LINE / PAL FOR MOMS