Bipolar Disorder
Level 2 Case
Trainee Guide

Contributors
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Pre-Assessment Learning

- Clark, C. T., Klein, A. M., Perel, J. M., Helsel, J., & Wisner, K. L. (2013). Lamotrigine dosing for pregnant patients with bipolar disorder. *American Journal of Psychiatry*, *170*(11), 1240-1247.
- NCRP general tenets of pharmacology in pregnancy

Optional Supplemental Reading

- Pinheiro, E., Wisner, K. L., & Clark, C. T. (2018). Quetiapine dose adjustments in pregnant and postpartum women with bipolar disorder. *Journal of clinical psychopharmacology*, *38*(1), 89.
- Deligiannidis, K. M., Byatt, N., & Freeman, M. P. (2014). Pharmacotherapy for mood disorders in pregnancy: a review of pharmacokinetic changes and clinical recommendations for therapeutic drug monitoring. Journal of clinical psychopharmacology, 34(2), 244.
- Bhella, V. S., & Garg, D. (2018). Use of liothyronine (L-T3) as an augmentation therapy for depression during pregnancy. *BMJ Case Reports CP*, *11*(1).
- Korevaar, T. I., Medici, M., Visser, T. J., & Peeters, R. P. (2017). Thyroid disease in pregnancy: new insights in diagnosis and clinical management. *Nature Reviews Endocrinology*, *13*(10), 610-622.

Overview
The goal of this module is to build upon core principles of treatment of individuals with Bipolar Disorder during the perinatal period. Relative to the introductory session in this module, this case has been designed to introduce additional complexity in the risk-risk equation of an overall treatment plan in addition to providing an overview of the use of lamotrigine during and after pregnancy.

This session is designed to last 60 minutes but can be modified for a longer or shorter session. The session is best utilized for psychiatry residents who have previously reviewed the introductory Bipolar Disorder module. Prior to the session, residents should read the articles included in the pre-reading section of this module.

Session

- **Clinical Vignette Part 1: read aloud (3 min)**
- **Discuss questions 1-3 (15 min)**
- **Clinical Vignette Part 2: read aloud (2 min)**
- **Discuss question 4 (5 min)**
- **Clinical Vignette Part 3: read aloud (3 min)**
- **Discuss questions 5-6 (10 min)**
- **Clinical Vignette Part 4: read aloud (2 min)**
- **Discuss questions 7-8 (10 min)**
- **Wrap up (10 minutes)**

Learning Objectives

1. Understand factors that influence the risk-risk discussion of pharmacologic treatment of perinatal individuals with bipolar disorder in complex treatment scenarios.
2. Consider pharmacodynamic and pharmacokinetic changes of pregnancy and their application to lamotrigine monitoring in the perinatal period.
3. Describe the current data informing the reproductive safety of second-generation antipsychotics during the perinatal period.
4. Review non-pharmacologic treatments of bipolar disorder and their application to the perinatal period.

Clinical Vignette Part 1

Ms. M is a 30-year-old G0 cis-gendered female who presents to you, a reproductive psychiatrist, for a pre-conception planning visit in the context of Bipolar Disorder Type 2. She and her husband would like to try to conceive in about 3 months. At present, she is utilizing an etonogestrel implant for contraception. She reports that her current medications have been working well for mood stability, and in fact she does not remember feeling this "level" for such a sustained period in her adult life. Her current psychiatrist, however, is uncomfortable continuing her current regimen during pregnancy. She has done some reading online about psychiatric medications in pregnancy and found your practice through an online search. She is excited to get established with someone "who understands the current data" and can treat her effectively during pregnancy.

Ms. M reports that she was initially diagnosed at age 14 with depression and has experienced recurrent depressive episodes since that time. Her depressive episodes have been characterized by a pervasive low mood, feelings of hopelessness, frequent tearfulness, increased appetite, decreased energy, decreased motivation, and low interest. She frequently experiences passive suicidal thoughts during depressive episodes: feeling that life is too hard to continue, or that those closest to her would be better off if she were gone. These episodes have typically lasted weeks to months; the last prolonged period of depression was about 5 years ago and in the context of trying to stop using tobacco.

In her 20s, Ms. M was diagnosed with Bipolar Disorder Type 2. Ms. M states that she realized herself that she experiences hypomanic episodes when she read about bipolar disorder in her college psychology class. She let her psychiatrist at the time know about her pattern of episodes, which lasted anywhere from 3 days to 2 weeks, where she would feel more self-confident, have more energy than is usual for her, would drink more alcohol, become more promiscuous and become very focused on exercise. She did very well in school during these periods as she could pull "all-nighters" without feeling tired. In retrospect, these episodes had been occurring since she was a teenager.

In more recent years, her primary concern has been difficulty managing her anger. She describes significant irritability and feels very easily overwhelmed. Describes herself as having "temper tantrums" where she yells, says "terrible things," feels physically agitated and at times has even thrown household items. Most often this has been directed towards her husband, or in her younger years, her parents. Ms. M has never physically harmed another person during one of these episodes, nor has she experienced a legal consequence related to her temper. She has, however, engaged in self-harming behaviors in the past in the context of intense agitation/anger. She hesitantly describes superficial cutting of her forearms and inner thighs to "just get me out of that state." Last self-harming episode was about a year ago. Describes irritability as a continued concern, however this has lessened considerably over the past year while on her current medication regimen.

Denies history of psychotic symptoms.

<u>Substance Use History:</u>

Ms. M reports that she uses nicotine (vape pen) several times per day and has had a very difficult time quitting. She has tried to utilize nicotine patches, however even when trialing a gradual, slow taper, she has experienced intense dysphoria fluctuating with mania. When asked to describe her manic symptoms in the context of tobacco cessation, she reports very high irritability, daily "temper tantrums," general feelings of restlessness and poor sleep.

On review of systems, she also endorses using medical cannabis products (edibles and tinctures) daily due to chronic pain from a previous motor vehicle accident. She drinks alcohol "occasionally," about 1 glass of wine 3 times per week.

Current Medications:
- Lamotrigine 200mg daily (started about 5 years ago, increased to current dose about 1 year ago)
- Oxcarbazepine 900mg daily (started 1 year ago)
- Aripiprazole 2.5mg daily (was taking up to 10 daily in the past but decreased due to irritability)
- Liothyronine 150mcg daily (for past 5 years, started for depression)

Psychiatric History:
Ms. M has been engaged in outpatient psychiatric medication treatment since early teenage years. She has intermittently engaged in psychotherapy, most consistently during college and graduate school. She has experienced passive SI and self-harming behaviors however has not had a suicide attempt. No inpatient treatment.

Previous medication trials include:
Several SSRIs (sertraline, fluoxetine, citalopram): all of these made her feel "all revved up, like I'm crawling out of my skin."
Bupropion: remembers this being helpful for depression in the past, not sure why it was stopped
Lurasidone: discontinued after 2 weeks at 20mg due to nausea.
Lithium: helpful previous treatment however after several months at 300mg daily dose, discontinued due to sedation
Quetiapine: trialed this at 25mg for insomnia; discontinued after the first dose as she woke up the next morning with a headache.

Family history: mother with alcoholism; maternal uncle "might" have bipolar disorder but hasn't been formally diagnosed.

Social History:
Childhood adversity: Ms. M reports that as a child, she always "had the necessities," and overall had a stable homelife. She reflects however that due to her mother's struggle with alcohol, her moods were unpredictable and at times she would be cruel and emotionally abusive. She experienced severe bullying in high school, an experience she correlates with the onset of her depressive episodes.
Traumatic events: About two years ago she was also in a serious motor vehicle accident. Another car suddenly pulled out in front of her in an intersection, and they collided. She reports chronic diffuse "all over" pain since this event.

Current social factors: Ms. M lives at home with her husband. They have been married for 3 years and overall have a supportive relationship however at times have struggled to communicate effectively. She has a "fine" relationship with her parents, who live about 2 hours away. She is an attorney. She has no guns in the home and no easy access to weapons. No legal issues.

Discussion Questions

1. Which aspects of Ms. M's history support the reported diagnosis of Bipolar Disorder Type 2? What differential diagnoses would you consider?

2. What risk factors and protective factors present in Ms. M's history might inform her risk for illness relapse during a future pregnancy?

3. Describe how Ms. M's overall presentation may inform a treatment plan? What components would this include? What specific advice would you offer regarding her medication regimen?

Clinical Vignette Part 2

At the first visit you discuss with Ms. M your overall clinical impression and proposed plan. You explore with her the timeline she presented, which included trying for conception in 3 months. You provide psychoeducation around the general tenets of disease management in pregnancy including minimizing polypharmacy, using lowest effective dose of medication, and selecting pharmacologic treatments based on likely efficacy, level of data (how *much* is known), and information concluded by the data (*what* is known). Ms. M expresses flexibility around her timeline for conception with a plan to prioritize finding a treatment regimen that she can continue throughout pregnancy. Medication treatment plan at the first visit is as follows:

1. Discontinue aripiprazole.
2. Re-trial nicotine replacement patch, starting with 21mg patch and reducing gradually every 6 weeks.
3. After brief period of monitoring off aripiprazole, begin taper of oxcarbazepine slowly (150mg every 2 weeks) with close monitoring.
4. Once oxcarbazepine taper is complete, will taper liothyronine. Will proceed in this "one step at a time" fashion so that the results of changes can be understood as specifically as possible.
5. As taper of oxcarbazepine, liothyronine, and nicotine cessation plan progresses, will continually evaluate need for increased lamotrigine or additional mood stabilizing medication.
6. Psychoeducation provided regarding cannabis use in the context of bipolar disorder and likely pregnancy. Motivational interviewing techniques are utilized. Ms. M reports she has a "close relationship with weed" and it feels overwhelming to consider cutting back or trying for abstinence given all the other changes that are discussed.

Ms. M returns for a series of follow-up visits on a every 2-week schedule:

- F/u #1: She has been off aripiprazole and utilizing a 21mg patch daily for two weeks and notices she is more emotionally reactive than previous, but otherwise OK. Laboratory results were remarkable for: TSH <0.015 mIU/L and T4 Free <0.10 ng/dL.
- F/u #2: Has started taper of oxcarbazepine. Is now on 750mg total daily dose. She is still on the 21mg nicotine patch. Reports in increase in anxiety, which is manageable at this point. Did have a visit with a therapist and thinks she might be a good fit.
- F/u #3: Stable with continuation of plan. No complaints.
- F/u #4: Is now on 450mg total daily dose of oxcarbazepine and 14mg nicotine patch. Ms. M reports an increase in irritability since last visit. States she wakes up every morning in a "terrible mood" and again started having "temper tantrums" daily. Feels physically restless and is sleeping only 3-4 hours per night. No active suicidal ideation. She is irritated that you are making her "give up" oxcarbazepine as a treatment option given how well it has worked for her in the past. While she was agreeable to the plan in the first visit, she states that "newer data shows it can be safe." She is surprised and frustrated that you are recommending discontinuation of something that works.

Discussion Questions

4. What would be your approach to this change described by Ms. M? What would you recommend at this point in her treatment?

Clinical Vignette Part 3

Ms. M proceeds with the plan for close monitoring and continual assessment of medication changes. After nearly a year, she is completely abstinent from nicotine and alcohol and has also considerably reduced cannabis use. She has been seeing a skilled therapist 1-2 times weekly who has helped her to process her previous traumatic experiences and to build emotional regulation and distress tolerance skills. About 10 months after your first visit, her ob/gyn physician removes her contraceptive implant. After another 3 months, you receive an urgent message from Ms. M via your electronic medical record patient portal system. She reports that she had a positive home pregnancy test the night before. Per her message, she is thrilled at this result however is "completely freaking out too." She asks, "which of my medicines should I keep taking now that I am really pregnant?" and "I am taking a prenatal vitamin but read on a blog post that I need to take high-dose folic acid too. Can you send that in for me?"

Ms. M's current medication are as follows:

- Lamotrigine 200mg daily
-Quetiapine 100mg AM and 300mg hs

Discussion Questions

5. What changes would you advise Ms. M to make now that pregnancy is confirmed?

6. Ms. M is taking lamotrigine 200mg. What prescribing considerations might you keep in mind during pregnancy? How would you respond to her question about high dose folic acid?

Clinical Vignette Part 4

Ms. M presents for a f/u visit at 28 weeks gestation. She is now taking a slightly higher lamotrigine dose (300mg daily) and remains on quetiapine 100mg am and 300mg hs. She has established with an ob/gyn practice and been adherent to all prenatal care recommendations. At her 20-week ultrasound she was enamored by seeing an image of her baby and reassured by the feedback from the maternal fetal medicine physician performing the ultrasound reading. At that visit she found out she is having a boy and she has decided to name him after her father. She has started taking childbirth, newborn care and "breastfeeding basics" classes through the local hospital.

Given how smooth her experience has been, she is surprised to report at her visit today that her mood has been "off." Again, she is feeling an increase in her energy level, "but not in a good way," and reports low mood, negative ruminations, and feelings of hopelessness that she has not experienced for a very long time. She denies any thoughts of suicide or self-harm but reports "I don't like the direction my mood is going." She is worried about her options as she knows she is "maxed out" on lamotrigine as she has read that doses over 300mg are associated with an increased risk for oral cleft malformations.

Discussion Questions

7. How might you address Ms. M's current depressive symptoms?

8. As Ms. M is entering her 3rd trimester, how might you approach planning for the postpartum period? Given her current medication regimen, what guidance would you provide around her desire to breastfeed?