NATIONAL CURRICULUM IN REPRODUCTIVE PSYCHIATRY

Reproductive Life Cycle

Clinical Vignette

Psychotropic Medication Interaction with Contraception

Facilitator's Guide

Contributors:

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Pre-Reading

- Oral contraceptives induce lamotrigine metabolism: evidence from a double-blind, placebo-controlled trial. Christensen J, Petrenaite V, Atterman J, Sidenius P, Ohman I, Tomson T, Sabers A. Epilepsia. 2007 Mar;48(3):484-9.
- Ethinyl estradiol, not progestogens, reduces lamotrigine serum concentrations. Reimers A, Helde G, Brodtkorb E.

Session Overview

- **Introduction to session and Case Discussion (20 minutes)**
- **Small group activity (20 minutes)**
- **Large group discussion: Take-home points (5 minutes)**

Learning Objectives

1. Learners will be able to discuss psychotropic medications and how they can affect metabolism of certain contraception.
2. Learners will be able to discuss birth control and its possible effect on a woman's mental health condition.

Case Scenario

Katherine Matthews is a 27-year-old single G0P0 graduate student with a long history of mood fluctuation, "rage," and impulsive behavior along with several documented episodes of depression characterized by irritability, sadness, anhedonia, social withdrawal, poor appetite, and suicidal ideation. Her symptoms first presented in adolescence, when she had two hospitalizations for suicidal behavior in the setting of substance use. She has been treated with low doses of various antidepressants, including sertraline, fluoxetine, and venlafaxine, all of which made her "edgy" and none of which was used for more than a few months. She has also tried aripiprazole 15 mg, which helped her mood but was associated with new-onset binge eating, and quetiapine, which "just made me fat and tired." She reports that her mood symptoms fluctuate mildly with her menstrual cycle, with increased irritability in the luteal phase.

Ms. Matthews' longtime therapist has been a stable presence in her life since college, and her symptoms have stabilized since she has been seeing you, the psychiatrist, for the past year. In your initial history, in addition to the above, you uncovered several discrete episodes of increased energy and productivity, during each of which Ms. Matthews felt fully rested on 3-4 hours of sleep a night. During these times she successfully submitted 12 applications for graduate school (though she had initially planned on only 4), planned an elaborate family vacation that was not realistic for her family and resulted in the family losing some non-refundable deposits, and spontaneously got in the car and drove 8 hours to pay a surprise visit on her college roommate.

Medical History: Non-contributory
Allergies: None
Family history: Ms. Matthews has a fraternal twin sister who suffers from PMDD, a mother with a history of postpartum depression, and a paternal uncle with bipolar I disorder.

FACILITATOR PAUSES FOR DISCUSSION

1. How would you characterize Ms. Matthews' illness?
- Elicit symptoms of depression and hypomania
- Elicit that illness is on the bipolar spectrum, with likely diagnosis given this information being bipolar II
- Review DSM-V criteria for bipolar II, which are:

Bipolar II Disorder
1. Criteria have been met for at least one hypomanic episode and at least one major depressive episode
2. There has never been a manic episode.
3. The occurrence of the hypomanic episode(s) and major depressive episode(s) is not better explained by schizoaffective disorder, schizophrenia, schizophreniform disorder, delusional disorder, or other specified or unspecified schizophrenia spectrum and other psychotic disorders.
4. The symptoms of depression or the unpredictability caused by frequent alternation between periods of depression and hypomania causes clinically significant distress or impairment in social, occupational, or other important areas of functioning.

2. What are some other key symptoms that will be important to determine in this patient?
- Disordered eating
- Substance use

Case Scenario Continued

Upon first meeting Ms. Matthews a year ago, you decided to start lamotrigine. The patient tolerated the medication well, and you successfully titrated the dose to 300 mg. She has been stable on this dose for the past 9 months, with a level of 7.7. Her mood has been stable and she reports no premenstrual irritability. She has recently decreased the frequency of her visits to once every three months, and you have been congratulating yourself on your expert diagnostic and treatment skills.
Today, however, Ms. Matthews presents in the clinic with garish lipstick, rapid speech, and is convinced that she has some "fantastic" ideas about how to fix the perennial scheduling issues in your office. Upon questioning, she reports that she has been sleeping only 3-4 hours a night for the last month, but "this is good, I'm not tired at all."

FACILITATOR PAUSES FOR DISCUSSION

3. What questions should you be asking at this point?
Facilitator elicits the following:
- Have there been any changes in her life – psychosocial stressors, shift work? Recent trip to Europe or other reason for jet lag/change in sleep?
- What is she using for contraception, and has that changed recently?
- Could she be pregnant?

Role Play Exercise

Facilitator solicits three groups of volunteers for doctor-patient role play (2 volunteers per group). Role play is conducted in front of a larger group, with each doctor-patient pair using scripts as outlined below (separate scripts will be provided).

Group 1: OCP Group

Patient: No shift work or plane trips! But I do have a new boyfriend, and I decided to start on the pill.
Doctor: Oh really? What kind of pill are you taking?
Patient: Oh, I can't remember the name of it.
Doctor: Do you know if it is a pill that has both estrogen and progesterone in it, or one with just progesterone?
Patient: I don't know. I think it was Ortho something.
Doctor: Did your doctor mention if it was called a "combined contraceptive pill"?
Patient: Yes, she did say that.
Doctor: Ok, I think I know what you're on. Tell me, when did you start the pill, and when was your last period?

Patient: Oh, I just started it when I got my last period, that was about a month ago.
Doctor: And when did your symptoms start?
Patient: Symptoms? What do you mean? I feel great!

FACILITATOR PAUSES FOR DISCUSSION

Facilitator elicits the following:

- Interaction between lamotrigine and estrogen-containing contraceptives.
- Estrogen decreases serum levels of lamotrigine
- Lamotrigine is metabolized primarily by glucuronidation by UGT1A4 and is renally excreted. Ethinyl estradiol is also glucuronidated by UGT1A4 and estrogens are known inducers of UGTs. The interaction thus leads to increased renal excretion of lamotrigine. Note that this is NOT a cytochrome P450 interaction!
- Theoretical differences in that interaction between monophasic or triphasic and during placebo week – monophasic have steady level of estrogen all month, so would expect symptoms stable across three weeks and different in placebo week; triphasic are up and down, so would expect fluctuation in symptoms. Lamotrigine half-life is about 37 hours, so these fluctuations could make a difference in symptoms – *though evidence to support this point is scant at best.*
- Benefits of continuous contraception in those on lamotrigine who use OCPs (no placebo week, so can adjust dose of lamotrigine and keep it stable throughout cycle)

Group 2: Implant Group

Patient: Well, I do have a new boyfriend, and I decided I should probably get serious about contraception. I got the implant.
Doctor: Oh really? When did you get that?
Patient: I think it was about three months ago.
Doctor: I see. Have there been any other changes in your life? Any big plane trips recently, or a new job?
Patient: I wish! I can't afford to go anywhere. I'm still doing part-time work at the coffee bar, but those hours are the same.
Doctor: And how are things going in grad school? Do you have a lot of work?
Patient: Yeah, it's been really intense. I'm finishing up my master's thesis this term, and I need access to this one special machine in the lab that's really booked up. The only time I can get on it is at 2 am, so I've had a lot of really late nights. At first that was awful, but I've totally gotten used to it – I feel like I have more energy now, not less!
Doctor: Ok, I think I know what's going on

FACILITATOR PAUSES FOR DISCUSSION

Facilitator elicits the following:

- While estrogen interacts with lamotrigine, progesterone does not
- List of progesterone-only contraceptives: Mirena, mini-pill, DepoProvera, Nexplanon
- Connection between shift work/sleep deprivation and onset of hypomania

Group 3: Pregnancy Group

Patient: Not really, I can't think of any major changes in my life. I don't have a steady partner, so I don't really use contraception, just condoms.
Doctor: Any changes to your job, or any travel lately?
Patient: Ha, I wish.
Doctor: What about your social life? Have you been sexually active recently?
Patient: Well, just once, and that was a few months back, a guy I met at a party.
Doctor: And did you use condoms that night?
Patient: Honestly, I can't remember.
Doctor: OK. This extra energy you have, and the decreased sleep – was that already going on back then, when you met this guy?
Patient: Oh no, that's just been for the last week or so.
Doctor: Do you think there's any chance you could be pregnant?

Patient: Well, I haven't gotten my period in a while, but I don't really keep track so I'm not sure how long it's been. I only had sex with the guy once, so how likely is that?
Doctor: I'd like to send you for a couple of tests.

FACILITATOR PAUSES FOR DISCUSSION

Facilitator elicits the following:

- Interaction between lamotrigine and estrogen in pregnancy
- What tests doctor wants to send patient for – pregnancy test and lamotrigine level
- Notion of the reference concentration in lamotrigine – desire to keep level in pregnancy at that pre-pregnancy stable concentration, with dose being raised accordingly as pregnancy progresses
- Relationship between mania/hypomania and unprotected sexual activity, importance of regular contraception in those with bipolar disorder

Wrap-Up

Facilitator asks individual groups to present their findings, ensuring that all points above under smaller groups are conveyed to the larger group.

References

Oral contraceptives induce lamotrigine metabolism: evidence from a double-blind, placebo-controlled trial. Christensen J, Petrenaite V, Atterman J, Sidenius P, Ohman I, Tomson T, Sabers A. Epilepsia. 2007 Mar;48(3):484-9.

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