

Reproductive Life Cycle

Progressive Case Conference Facilitator's Guide

Contributors:

Lucy Hutner, M.D., Washington Square Practice

Pre-Reading

- <u>The reproductive life cycle self-study materials</u>
- Deligiannidis K, Byatt N, Freeman M. Pharmacology for mood disorders in pregnancy. J Clin Psychopharmacol. 2014 April; 34(2): 244–255.
- Sramek J, Murphy M, Cutler N. Sex differences in the psychopharmacological treatment of depression. Dialogues in Clinical Neuroscience 2016 18 (4) 447-457.

Session Overview

The focus of this section will be on the basics of the reproductive life cycle in women. This case conference focuses on the knowledge of the reproductive life cycle impacts medical decision-making during pregnancy, postpartum, and breastfeeding. Topics such as the pharmacokinetic changes in pregnancy and sex differences in medication metabolism will be discussed.

- Discussion of self-study materials (10 min)
- Apply knowledge to a clinical case (40 minutes)
- Wrap-up/review (10 minutes)

Learning Objectives

Describe the stages of the menstrual cycle, including both biologic changes and their clinical impact
Compare the three trimesters of pregnancy and labor/delivery from a biological perspective and describe their clinical impact

3. Discuss the biological changes inherent in perimenopause and menopause and their potential clinical impact 4. Discuss specific differences in clinical decision-making in a pregnant patient, such as changes in metabolism and fluid shifts, that impacts medication prescribing

Case Scenario

Part 1: Preconception

Serena is a thirty-four year old woman with no active medical problems, with a history of generalized anxiety disorder, who presents for routine care to her psychiatrist. She is currently taking escitalopram 10 mg PO daily, which has been effective. She wishes to know if there are sex-related differences in the processing of medications and if that might affect her dose.

FACILITATOR DIRECTS DISCUSSION

1. If you were a trainee discussing this case with your supervisor, how would you describe the physiologic and pharmacokinetic factors that could influence sex differences in medication efficacy? *Facilitator elicits the following:*

a) Physiology

• Metabolic: body fat and weight distribution

• GI/Liver: gastric emptying, acid production, splanchnic blood flow, liver metabolism (e..g cytochrome CP450)

• Vascular: plasma volume, protein levels

• Endocrine: changes in physiology and hormone levels, interaction between estrogen and serotonin in the brain

• Renal: increased blood flow and GFR

b) Pharmacokinetics

• Small to moderate sex differences in all stages of pharmacokinetics, including drug absorption, distribution, metabolism, and elimination

2. How might you describe this to your patient in terms of specific recommendations regarding her medication regimen?

Facilitator elicits the following:

a) It is unclear whether sex differences influence medication response, mostly due to differences in study designs and the presence of confounding variables

b) There has been some indication that there may be variability in response to specific categories of medications, but the data is mixed (e.g. females may have a higher response rate to SSRIs than males, males may have a higher efficacy specifically with imipramine, there may be a higher efficacy of SSRIs in younger women vs women over 44)

c) There may be differences in side-effect profiles (e.g. sexual dysfunction) that might impact women and men differently

d) Different classes of medications must be considered separately, e.g. the adjunctive use of atypical antipsychotics in depression: need to consider issues such as metabolic changes and impact of changing prolactin levels

Reference: Sramek J, Murphy M, Cutler N. Sex differences in the psychopharmacological treatment of depression. Dialogues in Clinical Neuroscience 2016 18 (4) 447-457.

Part 2: Pregnancy

At a follow up appointment, Serena mentions that she had discussed with her partner the plan to start to conceive in the next year. She still has an intra-uterine device inserted. The psychiatrist and Serena discuss options regarding whether or not to stay on escitalopram during pregnancy and postpartum once she starts to try to conceive. After a detailed risk-risk discussion (as seen here in this optional 20-minute video, <u>Risk Conversation</u>), Serena elects to stay on this medication throughout pregnancy and postpartum. She then asks specifically about any dose adjustments that might need to occur due to pharmacokinetic changes in in pregnancy.

FACILITATOR DIRECTS DISCUSSION

1. If you were a trainee discussing this case with your supervisor, how would you categorize the pharmacokinetic changes that occur in pregnancy?

Facilitator elicits the following:

a) Situation is complex because of individual pharmacokinetic differences which may or may not have an impact on drug/metabolite levels

b) Even if there is a change in drug/metabolite levels, this may not be significant from a clinical standpoint (for example, the relationship between SSRI blood levels and efficacy isn't clear even though the blood levels likely vary during pregnancy)

c) Nevertheless, sex changes in pharmacokinetics described above may be amplified in pregnancy

d) Data do suggest that pregnant women may require higher doses of antidepressants, particularly in the later stages of pregnancy (e.g. after week 20). Women should understand that increasing medication dose is a function of pregnancy physiology, and that the patient should not feel she is "failing" because of the need for increased doses.

e) Broad variability among cases, but a trend toward faster metabolism of antidepressants suggests that it would be important to monitor clinical response and consider raising dose

f) Drawing blood levels is not recommended at this time (aside from TCAs)

g) Untreated depression and anxiety are risk factors for preterm birth and low birthweight, so there are both obstetric and pediatric reasons for treating maternal mental health (in addition to psychiatric reasons for the mother)

2. How specifically might this affect this particular patient, given the medications she is taking? *Facilitator elicits the following:*a) Carefully monitor clinically to watch for re-emergence of symptoms

b) Consider raising dose of escitalopram, particularly as pregnancy progresses, if clinically warranted; dosing may need to be increased more frequently than usual (every 2-4 weeks) due to a desire to achieve symptom remission BEFORE delivery if possible.

c) Would not routinely check blood levels aside from TCAs

d) Other medication categories, such as mood stabilizers, may require different interventions

Part 3: Postpartum

Serena attends a routine follow up visit with her psychiatrist at 35 weeks of pregnancy. Her pregnancy has been uncomplicated. Her mood is euthymic and she feels her anxiety has been well controlled on the current dose of escitalopram. She asks about the postpartum period and how this might affect her dose of medication.

FACILITATOR DIRECTS DISCUSSION

1. If you were a trainee discussing this case with your supervisor, how would you categorize the pharmacokinetic changes that occur in the postpartum period?

Facilitator elicits the following:

a) Postpartum state induces many physiologic changes, such as rapid decrease in sex steroids, contraction of plasma volume, changes in hepatic enzyme activity, and return to baseline GFR

b) Might increase overall blood levels, especially if an increased dose used in pregnancy is continued postpartum

2. How specifically might this affect this particular patient, given the medications she is taking?

Facilitator elicits the following:

a) Might manifest as adverse effects, due to drug toxicity

b) May need to lower dose back down, using pre-pregnancy dose as a guide

Reference: Deligiannidis K, Byatt N, Freeman M. Pharmacology for mood disorders in pregnancy. J Clin Psychopharmacol. 2014 April ; 34(2): 244–255.

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