NATIONAL CURRICULUM IN REPRODUCTIVE PSYCHIATRY

Primary Psychotic Disorders

Progressive Case Conference: Psychotic Disorders in Pregnancy

Facilitator's Guide

Contributors
Surya Sabhapathy, MD, MPH
Sarah Nagle-Yang, MD

Pre-assessment learning

Before you attend the classroom didactics on this module, please review some concepts of primary psychotic disorders during pregnancy in the following articles:

Vigod, S. N., Kurdyak, P. A., Dennis, C. L., Gruneir, A., Newman, A., Seeman, M. V., ... & Ray, J. G. (2014). Maternal and newborn outcomes among women with schizophrenia: a retrospective population-based cohort study. *BJOG: An International Journal of Obstetrics & Gynaecology*, *121*(5), 566-574.

Zhong, Q. Y., Gelaye, B., Fricchione, G. L., Avillach, P., Karlson, E. W., & Williams, M. A. (2018). Adverse obstetric and neonatal outcomes complicated by psychosis among pregnant women in the United States. *BMC pregnancy and childbirth*, *18*(1), 120.

NCRP Self-Study Module on Perinatal Psychopharmacology Decision-Making

NCRP Self-Study Module on Second Generation Antipsychotics

Optional supplemental reading:

Huybrechts, K. F., Hernández-Díaz, S., Patorno, E., Desai, R. J., Mogun, H., Dejene, S. Z., ... & Bateman, B. T. (2016). Antipsychotic use in pregnancy and the risk for congenital malformations. *JAMA psychiatry*, *73*(9), 938-946.

Miller, L. J. (1997). Sexuality, reproduction, and family planning in women with schizophrenia. *Schizophrenia Bulletin*, *23*(4), 623-635.

Ramsauer, B., & Achtergarde, S. (2018). Mothers with acute and chronic postpartum psychoses and impact on the mother-infant interaction. *Schizophrenia research*, *197*, 45-58.

Vigod, S. N., Seeman, M. V., Ray, J. G., Anderson, G. M., Dennis, C. L., Grigoriadis, S., ... & Rochon, P. A. (2012). Temporal trends in general and age-specific fertility rates among women with schizophrenia (1996–2009): a population-based study in Ontario, Canada. *Schizophrenia research*, *139*(1-3), 169-175.

Wan, M. W., Moulton, S., & Abel, K. M. (2008). A review of mother–child relational interventions and their usefulness for mothers with schizophrenia. *Archives of women's mental health*, *11*(3), 171-179.

Overview

The goal of this module is to utilize a clinical case presentation to solidify the learner's knowledge of the management of psychotic disorders during pregnancy. This session is designed to last 60 minutes but can be modified for a longer or shorted session. The session is best utilized for psychiatry residents who have some clinical experience with pregnant or postpartum patients. Prior to the session, residents should complete the required pre-reading this module.

Learning objectives
At the completion of this session, participants will be able to:

1. Understand the potential impact of antipsychotic medications on fertility
2. Describe how to approach decision-making around antipsychotic pharmacotherapy during pregnancy and breast-feeding
3. Discuss pharmacokinetic considerations during pregnancy and breast-feeding
4. Identify specific challenges that women with chronic psychotic disorders face when parenting

Resources required
1. A faculty (or senior resident) facilitator
2. Relevant articles for pre-reading

Session outline
1. Clinical vignette read-aloud: 5 min
2. Residents divide into working groups and discuss questions 1-3: 10 min
3. Facilitator-led large group discussion of questions 1-3: 10 min
4. Residents divide into working groups and discuss questions 4-6: 10 min
5. Facilitator-led large group discussion of questions 4-6: 10 min
6. Debrief and summarize take-home points from case: 5 min

Case presentation: Part 1

Crystal is a 32 y/o woman who was brought into the emergency room by the police after her friend Cathy called 911 with reports of bizarre and threatening behavior. Cathy states she was surprised today to find Crystal in her backyard; they haven't spoken in some time, and had made no plans for this visit. Per Cathy, Crystal told her that she needed to stay with her for a while. "She thinks her neighbors are messing with her, she's making no sense. When I told her I didn't think this was true, she began threatening me. She thought I was in on it too and told me she has a knife in her bag. I didn't know what to do, so I went back inside and called the police."

On interview, Crystal reports "my neighbors are harassing me, I can't go back there." She reports that her neighbors planted cameras and recorders in her house, and have been monitoring her for several weeks. As evidence, she relays that the neighbors strategically park their car on the street to get a view into her home. She also notes that they walk their dog by her house "more than once a day," and have been sending her coded threats by placing trash in her yard. She has been hearing strange sounds in her home which she attributes to the cameras. She is certain that they have been tampering with her food and reports "they don't fool me, I haven't eaten any of their poison."

When asked about her health history, Crystal appears guarded and asks "what does that have to do with anything?" In a cursory way, she denies any chronic mental or physical health conditions and states she takes no medications. She denies any history of pregnancy. She estimates her periods come "every few months" but isn't sure when her last menses occurred. She denies any previous surgeries. She smokes approximately 10 cigarettes a day and denies alcohol, cannabis, or other drug use. Crystal reports she lives alone but refuses to answer questions about employment, trauma, or sources of financial support. She denies suicidal ideation. When asked about the knife that the police did find in her bag, she reports this is for self-protection. "A girl has a right to protect herself!"

MSE: Crystal is an obese female, slightly unkempt and malodorous. She appears her stated age, and is guarded with intense eye contact. Her mood is anxious. Her affect is constricted but stable and

appropriate to context. Thought process is mostly linear and goal-directed, although at times she stops speaking suddenly mid-sentence without explanation. Thought content is notable for paranoid delusions and ideas of reference. She denies auditory or visual hallucinations but at times appears internally preoccupied during the interview. Crystal denies suicidal or homicidal ideation at the time of interview. She is oriented to person, place, situation and date. Insight and judgment are poor.

Through the medical record, Dr. B is able to identify an emergency contact to gather collateral information. Crystal's mother reports that she was diagnosed with schizophrenia at age 19. She had been an "A-B student" in high school and completed one semester of college before suddenly failing all of her classes. She returned home expressing paranoid beliefs and responding to voices. Her parents had suspected drug abuse, however when they brought her to the hospital, her urine toxicology screen was negative. She was admitted to psychiatry and eventually diagnosed with schizophreniform disorder. Since that time, she has had two additional psychiatric hospitalizations, both for acute psychosis characterized by delusions and hallucinations in the setting of non-adherence to treatment. During her last hospitalization, approximately 4 years ago, she was discharged on long-acting injectable paliperidone. With monthly injections, she has been free of delusions and hallucinations, though she continues to display negative symptoms such as lack of motivation, constricted affect, and reduced social interactions. Nonetheless, she has held down a part time job working concessions for a local professional sports team.

Over the past 2 months, Crystal has not kept in close contact with her family. Her mother states she isn't sure how Crystal has been doing more recently but was able to provide Dr. B with the name of the community mental health center where Crystal receives her care.

When Dr. B asks Crystal about paliperidone, she confirms she has been on monthly injections in the past, but can't remember the date of her last dose. Crystal reports that after her doctor left the agency for another job several months ago, she decided it would be too hard to "start over" – she instead decided to "give it a go without the shot." The community mental health center is closed for the weekend and staff will not be available for collateral until Monday morning.

Crystal's labs come back unremarkable other than a positive urine pregnancy test. The consulting obstetrician performs an ultrasound, confirming the pregnancy with an estimated gestational age of 16 weeks, 3 days. While Crystal reports the pregnancy is a surprise, she shows little reaction to the news and little interest during the ultrasound, asking only "can I go now?" When Dr. B reads the obstetrical consult note, she is surprised to read that Crystal reported two prior pregnancies to the obstetrician, stating she has two children ages 6 and 8 who are not in her custody.

Dr. B determines that Crystal requires psychiatric admission and completes the required paperwork for an involuntary admission.

Discussion Question

1. *How might Crystal's illness and associated treatment have affected her fertility and contraceptive planning?*

Elicit the following:

- Antipsychotics (particularly risperidone, paliperidone, and first generation antipsychotics) can cause hyperprolactinemia and subsequently reduce fertility.

- Crystal reports possible oligomenorrhea, suggesting hyperprolactinemia while receiving paliperidone injections. Discontinuing treatment may have resulted in resolution of hyperprolactemia and return to baseline fertility level.
- Overall, the fertility rate of women with schizophrenia is thought to be similar to that of the general population, and has increased in the past few decades due to increased use of second generation antipsychotics as well as deinstitutionalization of the severely mentally ill (Vigod 2012).
- Women with schizophrenia have higher-than-average rates of coerced sex, risky sexual behaviors, and unwanted pregnancies (Miller 1997). It should be noted however that sometimes women with schizophrenia will pursue intentional pregnancy, and it should not be assumed that her pregnancy is unplanned.
- Incorporating contraceptive counselling into mental health care delivery is an important tenet of reproductive psychiatry.
    - Consider long-acting reversible contraceptive methods like depot-medroxyprogesterone (q3month injection) or IUDs.
    - For women desiring tubal ligation, it is important to know the state laws regarding informed consent and restrictions in place to protect vulnerable populations from forced sterilization.

Case Presentation: Part 2

On Monday, the inpatient psychiatrist Dr. N calls Crystal's outpatient provider for collateral. Clinic records indicate that prior to paliperidone, Crystal had the following medication trials:

- Quetiapine (patient self-discontinued as it made her feel "like a zombie")
- Aripiprazole (uptitrated to 30mg, then discontinued given ineffectiveness)
- Haloperidol (discontinued due to cogwheel rigidity on exam)
- Ziprasidone (patient did not tolerate due to feeling "amped up").

Crystal's last paliperidone injection was 6 months ago. She has not seen a psychiatrist, case manager or other treatment provider since that time.

Crystal remains adamant that she does not need medications. Her family is extremely worried about her level of functioning, but also raises concerns about the effects of psychotropics on the baby.

Discussion Questions

2. *What factors might Dr. N consider when counseling Crystal and her family about treatment options? Please consider both the risks of untreated illness and potential risks of antipsychotic medication use?*
   (use the general pharmacologic tenets self-study as well as the SGA self-study if desired)

Elicit the following:

General Tenets of Psychopharmacology during pregnancy and postpartum:

- Risk of untreated or undertreated condition vs. risk of medication
- Consider: what is likely to be effective, how much data is available, what are potential side effects and what is the patient's preference?
- Lowest effective dose

- Avoid polypharmacy
- Maximize non-pharmacologic interventions
- Interdisciplinary communication is essential

Risk of the Disease:

- At baseline, chronic psychosis is associated with increased risk of adverse maternal and fetal outcomes compared to the general population. Untreated illness presents a potential "exposure" to the fetus.
- Pregnancy is not protective against acute or chronic psychosis. The risk of acute psychosis is elevated for a full 12 months post-partum.
- Outcomes generally associated with chronic psychosis (regardless of treatment status):
    - Obstetric: increased rates of C-section, induction of labor, longer length of hospital stay, placental abruption, and premature rupture of membranes (PROM)
    - Fetal: increased rates fetal distress, still birth, congenital malformations.
    - These outcomes may be confounded by baseline characteristics and rates of high-risk behaviors in this group:
        - increased rates of smoking, other substance use.
        - Medical comorbidities including diabetes, hypertension, obesity.
        - Poor prenatal care:
            - Less care overall due to low access or late discovery of pregnancy.
            - Difficulty adhering to recommendations due to positive or negative symptoms.
            - Social risk factors including increased risk of homelessness, susceptibility to domestic violence.
- Simple comparison of antipsychotic-exposed to unexposed pregnancies suggests increased adverse events at first glance, however:
    - Confounding by indication is a major issue: as above, psychosis is generally associated with increased risk; and pts with more severe illness are less likely to discontinue or decrease medication.
    - Studies that control appropriately for confounding (e.g. Vigod et al, 2014) are generally reassuring.

Pharmacologic-specific considerations:

- Crystal has had trials of haloperidol and several second generation antipsychotics with varying efficacy and tolerability. It would make sense to select an agent that is likely to be both effective and tolerable.
    - Potential options:
        - paliperidone (well tolerated and efficacious for this patient),
        - risperidone (theoretically has the same receptor profile as paliperidone),
        - lurasidone (not previously tried; relative lack of data, due to paranoia patient may not consume sufficient calories for medication absorption),
        - clozapine (need for requent laboratory monitoring, pt with multiple antipsychotic trials in past).
- Important to consider both the known risks of medications and the unknown risks associated with lack of data. Newer medications (i.e. lurasidone) typically have less data than older medications.
- A general tenant of perinatal psychopharmacology should be highlighted here: the most effective medication for the patient prior to pregnancy is likely to be effective

during pregnancy. In searching for a medication the psychiatrist should consider incorporate BOTH consideration of efficacy/tolerability AND safety.

- First generation antipsychotics and second generation antipsychotics are generally not considered teratogens but to have some associated obstetrical and neonatal risks:
    - First generation antipsychotics: potential risk of neonatal EPS.
    - Second generation antipsychotics:
        - likely increased risk of gestational diabetes; also gestational hypertension nd excess weight gain / obesity with some specific agents (i.e. olanzapine and quetiapine).
        - Associated with both small and large for gestational age infants.
    - Clozapine: monitor infant CBCs for possible agranulocytosis until 6 months after delivery. Contraindicated during breastfeeding (ongoing risk of agranulocytosis, seizure, etc).
- Placental passage varies between medications: highest olanzapine (72%), haloperidol (65%), risperidone (49%); lowest for quetiapine (24%; Newport 2007).
- Pharmacokinetic considerations.
    - Metabolism of antipsychotic medications is unpredictably affected by changes in hepatic metabolism.
    - Monitor patients closely for symptomatic change, and consider dose adjustments as pregnancy progresses.
    - If increasing doses are required during pregnancy, consider splitting into BID dosing. This extends the amount of time at which serum levels are above the minimum effective concentration, while minimizing time spent above the minimum therapeutic concentration (which would increase side effects without conferring additional benefit). If dose adjustments have been made during pregnancy, consider taper back down to the pre-pregnancy dose after delivery.

3. Consider an instance where Crystal becomes agitated in the emergency room during the evaluation period. How might her treating psychiatrist best manage her agitation?

Elicit the following:

Prioritize verbal de-escalation techniques, such as providing the patient with personal space, using a calm demeanor with a soft-spoken voice, identifying the patient's wants and feelings, and communicate in an honest, straightforward, transparent manner.

- In the situation where the patient does not respond to verbal de-escalation attempts and is engaging in behavior that puts her or other's safety at risk, medication may be necessary. Just as in non-acute settings, there is no "one best" medication to use in this situation, but the clinician must weigh available options in terms of likelihood of effectiveness, degree of information available about that option, and potential side effects to the patient.
- -In the rare situation when restraints are needed, careful positioning on the left side is essential for women in their 2nd or 3rd trimester of pregnancy in order to prevent vena cava syndrome.

Case presentation: Part 3

Crystal's family eventually convinces her to accept medications. After 7 days of inpatient treatment, she remains somewhat guarded, but no longer voices frank delusions and does not appear to be responding to hallucinations. As discharge planning progresses, the family confirms that Crystal does in fact have 2 children who have been in her sister's custody for several years. Crystal is initially somewhat reluctant, but eventually accepts her mother's offer to move back into the family home after discharge.

Discussion question

4. What post-discharge supports may be helpful for Crystal during the remainder of her pregnancy?

Elicit the following:

- Consider f/u with a reproductive psychiatrist, or subspecialty consultation for her current provider
- Provide links to resources such as MothertoBaby.org or OTIS.
- Ensure she is linked to outpatient obstetric followup.
- Consider support services such as case management, a doula, and/or home-visiting programs focused on transition to motherhood.
- Consider anticipatory guidance of child development and positive parenting practices during pregnancy.
- Plan early if a need for shelter or group home placement is anticipated; many institutions have restrictions on accepting pregnant women, or may only provide care through a certain gestational age.
- Consider overall support system in the analysis of safety and capacity for self care (i.e. may have differing expectations for discharge depending on what family supports are available).

Case presentation: Part 4

After discharge, Crystal receives outpatient obstetric care with Dr. Z. Her course is notable for erratic attendance at prenatal visits, along with periodic refusal of vitals and recommended blood work. When Dr. Z asks about fetal movement, Crystal often reports that she has no awareness of movement at all. She is sent directly from clinic to OB triage several times for periodic non-stress tests; all are consistently reassuring. Nonetheless, Dr. Z begins to feel uncomfortable about Crystal's ability to eventually parent her child and reaches out to Dr. A, Crystal's outpatient psychiatrist, for collaboration.

Discussion questions

5. How might Dr. A advise Dr. Z about approaching Crystal's challenges to prenatal care?

Elicit the following:

- Obtain ROI to facilitate involvement of Crystal's family, mental health treatment team, and other providers. Her support system is an important source of collateral, but can also help with understanding new information, keeping track of recommendations, and encouraging participation in treatment.

- Provide continued, clear education around signs of labor to both Crystal and her support system.
- Monitor closely for gestational diabetes and excess weight gain. Consider early referral to nutrition for prevention.
- If Crystal refuses testing or treatment:
    - Nonurgent issues: respect Crystal's autonomy, but inquire non-judgmentally about why she may be refusing some routine aspects of prenatal care.
    - Acute or imminent treatment needs: assess capacity to refuse treatment **at the time of refusal.** Emphasize to Dr. Z that a diagnosis of schizophrenia does not automatically negate capacity. It is important to assess the pt's ability to 1) communicate a choice, 2) understand relevant information, 3) appreciate the personal impact of the situation, and 4) provide rational explanation for her reasoning.
- Building trust and patient buy-in to treatment: these strategies may feel obvious to a psychiatrist, but are often not explicitly addressed in other medical fields.
    - Keep in mind that Crystal's ability to participate in care may be directly affected by symptoms of schizophrenia (whether positive, negative, or cognitive). Assume that she is doing the best she can at any given time.
    - When possible, be flexible about recommendations and maximize Crystal's sense of autonomy.
    - Exude transparency by offering clear and simple explanations for recommendations. It may help to acknowledge that refusal (or deferring) is an option, but explain why that course may be risky.
    - Consider a clinic-wide policy regarding clearly outlining the OB's obligations regarding mandatory reporting. Women with SMI may otherwise feel specifically targeted, and if the discussion needs to happen later on, it's much easier if you've planted some seeds ahead of time. This policy should outline the OB's reporting obligations and be in accordance with state child protection laws and regulations. Once developed, the OB practice may choose to distribute this to patients along with other routine information about the practice (i.e. after-hours contact information, instructions for accessing the practice for routine questions) and/or post the policy clearly in the waiting room. Be especially clear about any policies or legal requirements related to drug screening.
    - Provide education to clinical and support staff about schizophrenia to help minimize any stigma.

6. How might Drs. A and Z approach safety/disposition planning for after Crystal delivers her baby?

Elicit the following:

Most mothers with schizophrenia do raise their children and it is important to note that as with other mothers, a woman with schizophrenia is likely to value her identity as a mother and to want to feel competent in this role. At the same time, women with schizophrenia are likely to difficulties in parenting and additional supports may be needed. In general, successful parenting in women with Schizophrenia is more likely to occur with higher levels of family support and financial and social resources.

In general, Crystal may continue to face many of the same challenges to parenting as she did during prenatal care. Drs. A or Z may consider a referral to an infant mental health specialist or other parenting intervention which focuses on infant attachment and maternal sensitivity. It is important to note that while individual psychotherapy is a more conventional and accessible treatment methodology, enhancing maternal sensitivity requires a dyadic approach. Some examples of dyad-focused interventions that may be illustrated to learners are listed below, although it should be noted that these interventions have been studied primarily in women with other types of mental illness (i.e. MDD, GAD, PTSD) or in mothers of highly-reactive infants and have NOT been studied in women with Schizophrenia specifically. Parenting interventions for women with Schizophrenia remains an under-studied area of research.

- Circle of Security (group-based)
- Mom Power (group-based)
- Minding the Baby (home-visiting program)
- Parent-infant-psychotherapy (individual therapist works with dyad)

Some additional considerations:

- Legal and custody concerns:
  - Most child protection service agencies will not accept reports until the child is born.
  - In cases of agency involvement, the mother's housing may be complicated by whether she's legally allowed to live with her child. Families may have to decide whether to accept custody of the baby or provide ongoing support for the mother.
  - Substance use (even if marijuana only) may complicate custody case.

- Negative and cognitive symptoms may especially impact infant care:
  - Infant care is complex and difficult to manage (especially when sleep deprived) – pts may have trouble coordinating medical appointments for both mom & baby, mixing formula, etc.
  - Avolition and apathy may increase risk of poor response to the infant's crying or other needs; and limit active engagement of Crystal's support system.
  - Blunted affect may lead to downstream difficulty with mother-infant bonding (mother likely to be less emotionally reactive or expressive with the infant).

- Pharmacologic:
  - Antipsychotic-induced sedation may limit her capacity to provide regular overnight care and feedings.
  - Be especially mindful of assistance with ceasing tobacco use in this population; also know that nicotine replacement may affect metabolism of antipsychotics like olanzapine and clozapine.
  - Most psychotropics pass into breast milk; see MothertoBaby.org for good summaries.

Additional References for Dyadic Interventions:

Lieberman, A. F., Silverman, R. O. B. I. N., & Pawl, J. H. (2000). Infant-parent psychotherapy: Core concepts and current approaches. *Handbook of infant mental health*, *2*, 472-484.

Marvin, R., Cooper, G., Hoffman, K., & Powell, B. (2002). The Circle of Security project: Attachment-based intervention with caregiver-pre-school child dyads. *Attachment & human development*, *4*(1), 107-124.

Muzik, M., Rosenblum, K. L., Alfafara, E. A., Schuster, M. M., Miller, N. M., Waddell, R. M., & Kohler, E. S. (2015). Mom Power: preliminary outcomes of a group intervention to improve mental health and parenting among high-risk mothers. *Archives of women's mental health*, *18*(3), 507-521.

Slade, A., Sadler, L., De Dios-Kenn, C., Webb, D., Currier-Ezepchick, J., & Mayes, L. (2005). Minding the baby: A reflective parenting program. *The Psychoanalytic study of the child*, *60*(1), 74-100.