NATIONAL CURRICULUM IN REPRODUCTIVE PSYCHIATRY

Attention-Deficit Hyperactivity Disorder

Media Conference

Facilitator's Guide

Contributors

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Overview

Popular media frequently touches on issues germane to reproductive psychiatry and pregnancy, such as pregnancy weight gain, postpartum depression, stress in pregnancy, and breastfeeding. Well-known celebrities such as Gwyneth Paltrow and Chrissy Teigen have voiced their experiences with maternal mental health to millions of people worldwide. However, the tone of the messages arising from the media can be tinged with stigma. The ability to field patient questions arising from popular culture is an important professional skill for all psychiatrists. In particular, psychiatrists should be able to explain data and statistics cited in the lay media in an accurate, reassuring, and clinically relevant manner. Thus the goal of the NCRP's media modules is to have psychiatrists and psychiatry trainees build communication skills that enable them to serve as knowledgeable and thoughtful representatives of reproductive psychiatry to a lay audience.

Each session consists of three parts: 1) reviewing and critiquing a piece from the popular media (such as from newspaper articles or social media); 2) appraising the comparable medical literature; and 3) role-playing a psychiatrist/patient interaction about how to communicate this topic to a lay audience.

The aim of reviewing the medical literature is to compare its findings with the information portrayed in the media. For the purposes of this exercise, the most relevant parts of medical literature are the abstract, the introduction, and the discussion. The aim is not to have an in-depth, "journal-club" analysis of the article (which is an important skill for residents to master elsewhere in their training), but rather to delineate in broad strokes the gaps between the information presented by the media portrayal and by the medical literature.

Sessions usually last 50 minutes, but can be modified, depending on the number of media items and articles selected. The media conference is tailored for PGY-4 psychiatry residents but can be modified for any group of psychiatric providers. A small group setting with time and space to work within break-out groups is recommended. After review of the media items and the medical literature, the group will divide up into small groups of 2-3 participants to role-play the clinical interaction.

Session

Presentation of media items (10 minutes): Faculty and residents together will review the media item (s)

Review of medical literature (10 minutes): Faculty and residents together will briefly assess the comparable medical literature

Role-play with case example (15 minutes): Small groups of residents will role-play a psychiatrist/patient discussion

Large group discussion (10 minutes)

Wrap-up and Q+A (5 minutes)

Learning Objectives

1. Understand the power of the media to shape attitudes toward and concerns about attention-deficit/ hyperactivity disorder (ADHD) in pregnancy
2. Understand management and treatment recommendations for peripartum ADHD

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Resources Required

- A faculty moderator
- Samples from media (provided)
- Relevant article references (provided)
- Laptop (with internet access) and projector

Selection of Content

Content can either be selected in advance or selected at the time of the session. The faculty and resident group may pre-select a topic that is of particular interest to the group and distribute the media item and the article one to two weeks prior to the session. Alternatively, if there is a media item of particular interest to one or more of the trainees, they can bring the item to the session and the relevant literature can be appraised in the session in real time by the faculty and trainees, using a laptop and projector.

The media conference presented here, as part of our "ADHD Module," focuses on diagnosis, treatment, and overall management of attention-deficit/hyperactivity disorder during pregnancy; topics more directly relevant to reproductive psychiatry are included in media conferences in other subject areas (including perinatal depression, etc.).

Presentation of media items

https://edition.cnn.com/2017/12/13/health/adhd-drugs-pregnancy-safety-study/index.html

Critique of media coverage

1) What is the central claim of this media piece?
   Facilitator elicits the following:
   - ADHD medications (methylphenidate) taken during pregnancy increase the risk of heart defects

2) How do these media pieces influence (and potentially bias) the lay reader?
   Facilitator elicits the following:
   - Methylphenidate can cause heart defects; therefore, using stimulants during pregnancy is dangerous
     - "The attention-deficit hyperactivity disorder drug methylphenidate is associated with an increased risk of heart defects in infants whose mothers take the medication during pregnancy, according to a study published…in the journal JAMA Psychiatry. Researchers found a 28% increased prevalence of cardiac malformations after first-trimester exposure to the stimulant"
   - Doctors have increasingly prescribed ADHD medications to adults at a startling rate, and pregnant women could fall victim to this trend
     - "The use of these medications has increased by almost 800% between 1995 and 2015 among adults – including women of reproductive age."
   - Everyone in the scientific community agrees with the conclusions drawn from this study (implied by quoting one other researcher in the article)
     - "Dr. William O. Cooper, a pharmacoepidemiologist at the Vanderbilt University School of Medicine, reviewed the research and wrote an editorial in JAMA Psychiatry. The new study used 'appropriately rigorous methods,' said Cooper, who was not involved in the research… 'These results make an important contribution to the question of the safety of methylphenidate and amphetamine use during pregnancy.'

3) What are the scientific facts and statistics that the article uses to support its claims, and what are the potential problems we identify with those facts?
   Facilitator elicits the following:
   - Claim 1: Methylphenidate increases risk for cardiac malformations in babies
     - Quote: "…According to a study published Wednesday in the journal JAMA Psychiatry…the researchers found a 28% increased prevalence of cardiac

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malformations after first-trimester exposure to [methylphenidate]… 'If pregnant women take methylphenidate during the first trimester of pregnancy, they have a small increased risk of having a baby born with a cardiac malformation,' Huybrechts said.' "
    - Problem: In the study, the association between cardiac malformations and methylphenidate use did not end up being statistically significant after adjusting for confounders (eg, comorbid psychiatric illness)

- Claim 2: Methylphenidate causes a large increase in risk for cardiac malformations in babies
    - Quote: " 'The risk of a cardiac defect appears to increase from 10 per 1,000 births to about 13 per 1,000 births when the mother used methylphenidate during pregnancy,' Huybrechts said."
    - Problem: This suggests that cardiac defects are common; in fact, they are fairly rare, and this theoretically increased risk does not have clear clinical significance
- Claim 3: Pregnant women are 8x more likely to be on a stimulant for ADHD than they used to be
    - Quote: "The use of [ADHD medications] has increased by almost 800% between 1995 and 2015 among adults -- including women of reproductive age, one study finds."
    - Problem: This study is only from a UK cohort, the "800%" is a pooled number and does not pertain to pregnant patients per se, and it does not account for medication nonadherence (so the number of prescriptions is not a parameter to measure sustained exposure)

Appraisal of Scientific Literature

Huybrechts KF et al. Association between methylphenidate and amphetamine use in pregnancy and risk of congenital malformations: a cohort study from the International Pregnancy Safety Study Consortium. JAMA Psychiatry. 2018.

1) What is the study design? What 'level' would this study design be? What are the strengths and limitations with this study design?
   Facilitator elicits the following:
    - Study design: Cohort
    - Level of Evidence: IIb
    - Strengths:
        - Large size
            - A total of 1,813,894 publicly insured pregnancies in the United States and 2,560,069 singleton pregnancies in the 5 Nordic countries ending in live births were included
                - In terms of exposures, the study included 2,072 infants exposed to methylphenidate and 5,517 infants exposed to amphetamines in the US cohort; 1,402 infants (0.05%) were exposed to methylphenidate in the Nordic countries cohort
        - Data from two major world regions: US and northern Europe (Denmark, Finland, Iceland, Norway, and Sweden)
        - Exposure and outcome data were independently and prospectively collected (mitigating recall bias)
        - Rigorous inclusion criteria:
            - For example, used more specific definition of medication exposure (medication had to be dispensed twice), accounting for medication nonadherence as possible confounder
        - Rigorous exclusion criteria:
            - For example, excluded pregnancies with exposure to known teratogenic medication in first trimester, as well as pregnancies with known chromosomal abnormality

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- Adjusted for many confounding variables, including demographic characteristics (age, race/ethnicity, year of delivery), obstetric characteristics (multiparity, multiple gestations), psychiatric conditions, chronic comorbid medical conditions, markers of general comorbidity, and prescribed medications
- Limitations:
  - Nonrandomized → residual confounding
  - Included only live births → selection bias and underestimation of relative risk (excluded possible association with non-live births)
  - Did not account for ADHD severity → residual confounding (falsely inflated risk of malformations in exposure group)
  - Small number of pregnancies with exposure to amphetamines in Nordic cohort → insufficient power to assess risk associated with amphetamine exposure in Nordic cohort
  - Definition of cardiac malformations was more narrow (excluded patent ductus arteriosus, patent foramen ovale) → possible underestimate of relative risk
  - Limited demographics – U.S. cohort consisted exclusively of Medicaid patients, and European cohort consisted only of Nordic populations (which tend to be more homogeneous ethnically and socioeconomically)
  - Strange wording: "results suggest a small increased risk of cardiac malformations associated with methylphenidate use"

2) What are the central findings of this article?
Facilitator elicits the following:
- This study does not demonstrate a statistically significant difference in risk for congenital malformations among infants exposed to stimulants compared to those who are not
  - When the researchers controlled for potential confounding factors, including maternal psychiatric illness, the findings of increased risk were no longer observed in either cohort. In the U.S. cohort, the adjusted relative risks for exposure to methylphenidate were 1.11 (95% CI, 0.91-1.35) for any malformation and 1.28 (95% CI, 0.94-1.74) for cardiac malformations. In the Nordic cohort, the adjusted relative risks for exposure to methylphenidate was 1.28 (95% CI, 0.83-1.97) for cardiac malformations. Given that the confidence intervals include 1, these findings are **not** statistically significant.
  - Results from pooled data (both U.S. and Nordic cohorts) showed a borderline statistically significant association between methylphenidate and cardiac malformations (relative risk of 1.28 with 95% CI, 1.00-1.64).
    - In the U.S. cohort, even before controlling for confounding factors, amphetamines were not associated with increased risk for cardiac malformations (unable to draw conclusions in the Nordic cohort due to small number of pregnancies with exposure to amphetamines)
    - ***This differs from the wording of the article, which says that this study *suggests* a small increased risk of cardiac malformations associated with methylphenidate use
- If there is a possible increased risk, the increase is very small
  - In this study, risk for cardiac malformation was 1.27% in the unexposed group and 1.63% in the exposed group – the clinical significance of this increased risk is unclear

Role-playing Exercise

Trainees should separate into groups of 2 or 3 with one trainee playing the role of the physician, one the patient, and others as observers or family members.

Sample Clinical Case

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Ms. C. is a 29yo woman, G1P0 at 10 weeks gestation, married for 3 years, working in financial services, with a history of attention-deficit/hyperactivity disorder (ADHD) and generalized anxiety disorder (GAD) for which she used to take Concerta 54mg and sertraline 150mg with good control of symptoms, who has discontinued both Concerta and sertraline at the recommendation of her Ob Gyn because of pregnancy. She reports no history of suicide attempts or hospitalizations, and is presenting with several weeks of difficulty focusing, worsening anxiety, and rising tensions with her husband due to staying late at work to finish her tasks for the day.

Ms. C. says that her ADHD was diagnosed in early high school, though she recalls having difficulty focusing going back to her pre-teen years. She says her anxiety also emerged at around the same time, in the context of worsening school performance. After trialing Adderall IR and Adderall XR, she noted some improvement in her symptoms using Ritalin IR two times per day. She was then prescribed Concerta, which yielded the most improvement in symptoms at a dose of 54mg. Her anxiety was also reduced somewhat after stimulants, however she reports a significant reduction in her anxiety after adding sertraline (in her early 20s). She had been maintained on Concerta 54mg and sertraline 150mg until she found out she was pregnant, and at her Ob Gyn's recommendation, tapered the medications and was off completely approximately 3 weeks ago. She says she felt well for about 1 week, but then in the last 2 weeks started to notice increased difficulty focusing, such that it now takes her almost twice as long to finish reading long reports at work. She says her mind "goes all over the place" while she is trying to complete tasks at work, finds herself "going down a Google rabbit hole" instead of focusing on her task. She has also become more anxious in this context, is constantly worried about her pregnancy and ability to maintain her position at work. She also says her sleep has been more restless, and that she has new muscle tension. She now feels tired during the day, and she finds it increasingly hard to leave work at a reasonable hour. She gets home so late sometimes that she has not been getting a full night's sleep. Her husband has also become upset several times when she arrives home much later than she said she would. She is concerned that she will be fired, and wonders if this pregnancy was "worthwhile."

On ROS, Ms. C. denied depressed mood, changes in appetite, elevated mood, decreased need for sleep, recent or past substance use. She underwent lab testing at the recommendation of her Ob Gyn and was told that her thyroid hormone was within normal limits. She denied other medical problems.

Sample Script for the Physician
"It sounds like things have been really hard for you in recent weeks. I am most struck by your difficulty concentrating, to the extent it is taking you much longer to complete tasks at work, leading to longer work hours, less sleep at night, and tensions with your husband. You're also now worried you may lose your job, and are feeling more anxious overall. It seems like a lot of these troubles stem from your attentional difficulties – similar to many years ago, when things came together for you after you could improve your focus. It is not unusual for pregnant patients with ADHD to stop their medication in pregnancy, and it is understandable that you and your Ob Gyn thought it was a good idea. However, we're seeing the downstream effects, and therefore it is important to address your ADHD symptoms given their significant impact on you, your work, and the people around you. Fortunately, there are many treatment options for ADHD, including medication and other non-pharmacologic approaches."

Patient then asks a series of questions:

1) What are the treatment options for ADHD?

- "There are many treatment options for ADHD, including medications and other non-pharmacologic options. Medications include stimulants, such as Ritalin and Adderall, and they can be divided into short-acting agents and long-acting agents. Choice of a particular stimulant, and short- versus long-acting, depends on the needs of the patient, as well as how well they tolerate it and whether it has been effective. There are other non-stimulant medications that work through a different mechanism; they are used less frequently, but are sometimes excellent options if the stimulants are not effective or are not tolerated well. Among non-pharmacologic options, cognitive-behavioral therapy (CBT) for ADHD focuses on improving behaviors, specifically self-control and self-mediation. This can be done in an individual or group format. We have less literature on the use of CBT for ADHD compared to stimulants, but it is widely considered a valuable tool. Finally, other treatment options include lifestyle changes, such as decreasing or modifying one's work responsibilities, as well as instituting specific rules and routines in one's

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day-to-day life in order to stay organized (often with the help of loved ones). While not a formal 'treatment' option, these lifestyle changes can be very helpful for patients with ADHD."

2) Do I have to take medications for my ADHD?

- "The decision to take a medication depends on the patient – namely, the severity of their symptoms, their history of treatment response, and the nature of their day-to-day tasks requiring sustained attention. In cases where symptoms are less severe, and/or there is significant room to modify or decrease one's daily tasks requiring attention, one can try a non-pharmacologic approach like CBT and/or lifestyle modifications. In other cases where symptoms are more severe, the day-to-day tasks requiring attention are intense and unmodifiable, and/or the effects of symptoms are profound (one's job is on the line, or social relationships at risk), then one would more strongly consider medication. In your case, it seems that the potential implications of your symptoms are significant, indicating a more severe case, however we have not discussed how you might be able to try CBT, or modify your work responsibilities/daily routine to accommodate your symptoms. If these lifestyle changes, or CBT, are not possible, then medication would be a better option. It is reassuring to know that you have tried medication before, tolerated it well, and knew that it worked for you. In that sense, if we were to use medications you used in the past, we would not be wasting time exposing you (and baby) to a medication that may not work, or causing problematic side effects. That being said, we should also discuss the risks of such medication in pregnancy."

3) What are the risks associated with taking ADHD medications in pregnancy?

- "For the time being, we will focus on the fetal risks associated with stimulant medications, which are the more commonly prescribed medications for ADHD, and are the medications I would consider prescribing for you because you responded well to them in the past. Regarding the risk profile of methylphenidate (which is the main compound in Ritalin IR and Concerta – both of which you had used in the past), data is limited but expanding. As with all medications in pregnancy, particularly psychotropics, data is limited by the nature of the research; it is unethical to do randomized controlled trials (the research gold standard) in pregnant women. As such, the data is in the form of case studies/case series and cohort studies, many of which are limited by confounding variables. Keeping this in mind, the data thus far on methylphenidate has not shown a statistically significant increased risk for congenital malformations in infants whose mothers were on medically indicated doses. A US Medicaid Study found an association with pre-eclampsia (in mothers who filled prescriptions twice), and a secondary analysis found an association between methylphenidate and amphetamines with preterm birth; however, confounding variables were not accounted for, and could explain these results. Similarly, a study of NICU admissions found an association with methylphenidate, however the authors felt that these results could also be explained by confounding variables (obesity, cigarette smoking, and other psychotropic use in this case). Thus, the data thus far is reassuring, but is limited and therefore stimulants should be prescribed on a case-by-case basis.

Wrap-up and Q+A

1) For the learner role-playing the physician: what was challenging about this interaction?

- Managing the patient's anxiety
- Tailoring psychoeducation in a way such that sufficient information is provided, but not too much
- Feeling confident in explaining the medical literature to a patient

2) For the learner role-playing the patient: what was challenging about this interaction?

- Understanding the nuance of prescribing medication in pregnancy
- Understanding the complexity of data from pregnancy research
- Accepting that there is no right answer

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