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Translating science into care

The National Perinatal HIV Hotline 2019 CROI Roundtable Discussion
ARV Selection for People of Childbearing Potential
March 6, 2019 CROI Seattle, WA

The National Perinatal HIV Hotline (www.nccc.ucsf.edu) hosts roundtable discussions at CROI to promote dialogue around challenging topics and build community among providers. Discussion notes are distributed via the ReproIDHIV listserv. For more information: marliese.warren@ucsf.edu

In May 2018, an unplanned interim analysis from the Tsepamo study in Botswana showed a possible increased risk of neural tube defects among infants born to women who were taking dolutegravir at the time of conception. This followed on the heels of data suggesting that antiretroviral regimens containing elvitegravir and cobicistat might not achieve adequate drug levels to maintain virologic suppression in late pregnancy. As the list of antiretroviral medications considered safe for use at conception and during pregnancy is increasingly divergent from the list of preferred agents for non-pregnant adults in United States guidelines, providers and patients are left asking themselves and each other how to proceed. The 2019 CROI roundtable was an opportunity to discuss the use of antiretrovirals in people of childbearing potential and in pregnancy. Roundtable participants divided into three groups. Each group was guided by a case and discussion questions and facilitated by one physician and one community member living with HIV. We took notes on the discussions and coded key points into major themes, which are outlined below. The cases and discussion questions can be found in an appendix at the end of the notes.

A note on language: We acknowledge that not all people who get pregnant and give birth identify as women and not all people who identify as women can or will get pregnant and give birth. We made an effort to use gender-inclusive and person-first language throughout this document.

Patient-centered conversations:

Each group stressed the importance of engaging patients in a discussion about options for HIV treatment and prevention. Roundtable participants had many ideas about how to support patient-centered decision making.

- Engage the patient in a discussion with the goal of arriving at a shared decision. Providers can inform patients and provide evidence.
- It is vital to share as much information as possible with patients in order to support an informed choice.
- Listen carefully to clients' concerns, desires and experiences.
- Guidelines are just that – guidelines. They are not the law.
- How and when to have a child is a very personal decision. For patients in serodifferent relationships (where one partner is living with HIV and the other is not), decisions about using PrEP, ovulation detection kits, etc. should be up to the couple. The provider's role is to offer information about options to help individuals make decisions.
- Emphasize the positives – stress the things that individuals and couples are already doing for themselves, their health, and their potential future child.

In light of the new data about dolutegravir, providers needed to find a way to convey the potential risk of neural tube defects to patients taking dolutegravir who might get pregnant. Roundtable participants had suggestions about how to best promote patient-centeredness in these discussions:

- Avoid scare tactics but provide a balanced view of risk and uncertainty.
- Information needs to be accessible to a lay audience and may need to be provided over several sessions to provide patients with time to process information and decisions.
- Provide handouts in simple language for patients to review on their own time. Offer follow-up discussions and sufficient time for questions. Providers might want or benefit from standardized "scripts" to use with patients.
- Be aware that conversations may evoke strong emotions/reactions.
- Feelings about pregnancy, or avoiding pregnancy, can be complex and multi-dimensional. A single question about pregnancy intentions, such as "Do you plan on getting pregnant in the next year?" is potentially helpful but may not be sufficient. For people who are not consistently using contraception, it can be helpful to ask follow up questions, such us "How would you feel if you were pregnant today?" to open up a more nuanced conversation about the risks and benefits of continuing dolutegravir.

Dealing with fear and mistrust:

Discussions about risks of a medication, especially a medication that a patient is already taking, might evoke fear and feelings of mistrust.

- It is important to establish trust as a basis for all conversations about medications and pregnancy.
- Stigma influences openness and communication, and people already experience a lot of stigma around HIV and reproduction.
- One participant shared a patient's reaction: "How am I supposed to trust you when you told me this was safe for me and now it is not?"
- Headlines from the press also influence the conversation that patients hear. They might hear about medication risks from media or social networks before they hear about it from a provider.
- Providers might have a fear of litigation that influences their own approach.

Participants suggested a helpful way to frame the discussion: "We're learning more and more, and that helps us to make better decisions. You will hear things and read things from other people and places, but I hope that you will discuss any concerns or things you hear with me, so that I can share what I know from the medical literature."

Life is risky:

There is no such thing as no risk in life or pregnancy. Pregnancy carries much uncertainty and risk by itself and all medications carry some risk. It is important that we be realistic about the size of the risk (as far as we know/understand). The patient's HIV status (or the HIV status of their partner) and the medications they are taking should not overshadow all of the other important aspects of optimizing health during pre-conception and pregnancy.

Medication changes can be hard and scary and emotional. For many people, the "devil you know is better than the devil you don't". Discussions are in the context of a lifetime of conversations about ARV use, often starting before pregnancy, and definitely continuing after birth.

Practical approaches:

Participants shared practical tips for caring for women living with HIV in the context of current data on dolutegravir and neural tube defects. One provider reviewed all medical records of their child-bearing age patients for women who were on a dolutegravir-containing regimen. They reached out via phone to those women to discuss the new information about dolutegravir and discussed changing regimens regardless of stated desire for pregnancy.

- Most patients, when provided the available information, chose to change their regimens.
- Some preferred dolutegravir and wished to stay on their current regimen.

Remember to utilize peer support and networks. Support is a group effort.

Some people will be planning for pregnancy or pregnant for many years (people who desire multiple children, people who are experiencing infertility, etc). Taking into account their personal history and antiretroviral resistance/exposure data and response, what are the antiretroviral options that a person can potentially take ***throughout*** their childbearing years, whether pregnant or not, without necessitating multiple switches?[1]

- Tenofovir/emtricitabine/rilpivirine (Odefsey or Complera)
- Tenofovir/emtricitabine/elvitegravir/cobicistat (Stribild or Genvoya): Need to follow viral load carefully in third trimester or change during pregnancy
- Tenofovir/emtricitabine (Truvada or Descovy) plus atazanavir and ritonavir — challenge is pill burden and side effects
- Tenofovir/emtricitabine (Truvada or Descovy) plus darunavir and ritonavir — challenge is pill burden, side effects, and going to twice daily darunavir/ritonavir once pregnant

There are single-tablet regimen options which do not include dolutegravir:

- Efavirenz-based (Atripla)
- Rilpivirine-based (Complera or Odefsey): Need to follow viral load carefully in third trimester

Advice for clear communication with patients:

- Listen carefully
- Provide clear, accurate information, in writing if possible
- View as an on-going discussion, not a one-time “information-dump”
- Acknowledge that clinicians and researchers don’t know everything, and that what we do know is changing (sometimes rapidly)
- Recognize that changing medications is hard
- Trust, language, and messaging are all important
- Avoid fear-based language
- Avoid stigmatizing language
- Use people-first language
- Remember that the choice is hers
- Allow sufficient time for decision-making

[1] The below regimens were options that providers participating in the discussion felt comfortable prescribing for non-pregnant patients who might get pregnant at some point in the future. These are not necessarily regimens recommended for starting in pregnancy.

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Discussion notes are distributed via the ReproID HIV listserv. The ReproIDHIV Listserv is a dynamic forum for clinicians and other healthcare professionals who specialize in reproductive infectious diseases. Participants use the forum to discuss clinical cases, share clinical approaches and protocols, network with colleagues, and arrange patient referrals. For more information, or to join the listserv, please contact marliese.warren@ucsf.edu.

As always, we are stronger together and there are many people who contribute to the success of our annual Perinatal HIV Roundtable. We want to offer our gratitude to:

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Appendix - Cases used for group discussion

Case 1

26 year old perinatally infected female G1P1 who transfers care from adolescent clinic. She is on tenofovir disoproxil fumarate/emtricitabine/rilpivirine and her CD4 count is in the 600 range. Her HIV viral load is < 20 copies/mL. She was on abacavir/lamivudine/dolutegravir during her last pregnancy and delivered a healthy baby in November 2017 (6 months prior to the unplanned analysis from the Tsepamo study). Her adolescent provider changed her after her last pregnancy off abacavir/lamivudine/dolutegravir due to the concern about dolutegravir and neural tube defects. She is interested in going back on abacavir/lamivudine/dolutegravir. She also probably wants to have another baby in the next year, but is feeling ambivalent. She is not interested in contraception.

Discussion Questions:

1. How do you approach the conversation about dolutegravir and the risk in pregnancy, especially when she was just recently delivered a healthy baby who was conceived while she was taking dolutegravir?

Women may spend many years in a potentially preconception or pregnant state.

2. How can we normalize this when it comes to conversations about ARV choices?
3. What are the options for ARVs that a person can take throughout their childbearing years?
4. What if this is a patient who is struggling with infertility? Does that affect your ARV choice?

Her partner was on PrEP during her previous pregnancy but is asking if he still needs it.
How do you involve couples or other HIV-negative partners in decisions about PrEP in the context of an undetectable viral load?

Case 2

36 year old female living with HIV at 18 weeks pregnancy referred to an HIV clinic for management. She was diagnosed with HIV 8 months ago and started on tenofovir alafenamide/emtricitabine and dolutegravir. She reports 100% adherence and her CD4 count is 400 range with viral load < 20 copies/mL. She first sought care in this pregnancy from her primary care provider when she was about 12-13 weeks pregnant by her last menstrual period. That provider changed her regimen to tenofovir disoproxil fumarate/emtricitabine and raltegravir twice daily, telling her that she shouldn't continue dolutegravir because of risk that her baby could have a brain defect. She often misses her second dose of raltegravir and her repeat viral load is now 250 copies/mL. She does not want to change back to dolutegravir because she is very concerned about the risk to her baby.

Discussion Questions:

1. Would you suggest a change of regimen?
2. How do you counsel her?
3. What ARV options would you discuss with her?

Patients living with HIV who are pregnant often have very little choice in their obstetric provider and delivering hospital. They often are asked to travel to a specialty center and see multiple providers.

4. How can we best support women to have a joyful, supported, and "normal" pregnancy in the context of HIV?

Case 3

32 year old female comes to see you because her male partner is living with HIV and they are interested in getting pregnant. She's on injectable medroxyprogesterone (Depo Provera) and they currently use condoms most of the time. He was diagnosed about 6 months ago and has been on ART (tenofovir alafenamide/emtricitabine/bictegravir) ever since. She thinks that his viral load has been undetectable. She has always tested negative for HIV, most recently 1 month ago. The last time they had sex was last night and they didn't use a condom. She wants to talk about the risks and benefits of taking ARVs for prevention of HIV acquisition.

Discussion Questions:

1. How do you discuss the options for HIV prevention while she and her partner are trying to conceive?
2. What about HIV prevention options during pregnancy and breastfeeding?
3. How do you involve couples or other HIV-negative partners in decisions about PrEP in the context of an undetectable viral load?
4. At what point should everyone feel comfortable with the patient stopping contraception and engaging in more regular/frequent condomless sex?
5. Would you recommend PEP now given that they had condomless sex last night? If so, with what ARVs?

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