Literature Review

National STD Curriculum Podcast

Doxycycline Prophylaxis to Prevent STDs

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Season 1, Episode 4

Doxycycline prophylaxis (pre or post) has been suggested as a way to prevent bacterial STIs [sexually transmitted infections] in high-risk groups and may be of interest in your patient population. This episode focuses on published literature on this topic.

Topics:

- doxycycline
- antibiotic prophylaxis
- preexposure or postexposure prophylaxis

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Disclosures
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Transcript

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In this episode:

[00:00] Introduction
Hello everyone, my name is Meena Ramchandani, I'm an infectious disease physician at the University of Washington in Seattle. This podcast is dedicated to an STD [sexually transmitted disease] literature review for health care professionals who are interested in remaining up-to-date on the diagnosis, management, and prevention of STDs.

[00:23] Background
I'd like to focus this podcast on the topic of using doxycycline to prevent bacterial STDs. This came up because a patient on PrEP, which is preexposure HIV prophylaxis, asked if he could take a prophylactic medication to prevent an STD, similar to how he takes PrEP to prevent HIV acquisition. STD prophylaxis (whether pre or post) seems to be something patients are interested in and I've heard this from other clinicians as well. The idea is interesting—a prophylactic medication a patient could take to stop an acquired infection before it becomes a disease—and seems to have potential value for both the individual in terms of decreasing their own personal rates of acquiring an STD, as well as the public health for decreasing the rates of STDs in the entire community.

The clinical community, though, is trying to reduce unnecessary antibiotic use and so one of the questions that comes to mind is, if we start using antibiotic prophylaxis, won't that increase antimicrobial resistance in a community? On the other hand, antibiotic prophylaxis for other diseases are used for extended periods of time—for example, doxycycline is used for long periods of time in the case of malaria prophylaxis or Lyme disease—and, resistance to doxycycline remains rare for both chlamydia and syphilis. Overall, it seems as though the topic is controversial and we're going to be hearing more about this as health care providers. Let's begin with the three articles I'm going to discuss on this topic.

[01:53] Paper #1

Bolan RK, Beymer MR, Weiss RE, Flynn RP, Leibowitz AA, Klausner JD. Doxycycline prophylaxis to reduce incident syphilis among HIV-infected men who have sex with men who continue to engage in high-risk sex: a randomized, controlled pilot study. Sex Transm Dis. 2015 Feb;42(2):98-103.
[PubMed Abstract]
The first article I'd like to discuss references a manuscript published in *Sexually Transmitted Diseases* in February 2015, so a few years ago. This article is titled "Doxycycline prophylaxis to reduce incident syphilis among HIV-infected men who have sex with men who continue to engage in high risk sex: A randomized, controlled pilot study," published by Dr. Robert Bolan and his colleagues in Los Angeles.

1. This is a small study enrolling just 30 MSM [men who have sex with men] with HIV.
2. Participants were randomized to doxycycline PrEP, preexposure prophylaxis. They were receiving the medications daily; they received either oral doxycycline 200 mg daily for 48 weeks, which is a bit of a high dose. So, these participants were randomized to doxycycline PrEP, preexposure HIV prophylaxis, and they received either oral doxycycline 200 mg daily for 48 weeks for prevention of STDs versus—and this is interesting—a contingency management with a financial incentive for remaining STD-free.
3. What they found in this small study is that subjects receiving doxycycline were significantly less likely to test positive for any STD rather than the financial incentive for remaining STD-free.

Now, the impact of doxycycline on the transmission of each bacterial STD (gonorrhea, chlamydia, or syphilis) was not significant, but given the size of the population, it's not really surprising. There was an overall reduced STD acquisition at week 48 in this group, which I think is compelling. And the promising results of this article lead me into the next study, which describes using doxycycline as postexposure prophylaxis [PEP], and this manuscript was published a few years later in 2017.

[03:47] Paper #2

Molina JM, Charreau I, Chidiac C, Pialoux G, Cua E, Delaugerre C, Capitant C, Rojas-Castro D, Fonsart J, Bercot B, Bébéar C, Cotte L, Robineau O, Raffi F, Charbonneau P, Aslan A, Chas J, Niedbalski L, Spire B, Sagaon-Teyssier L, Carette D, Mestre SL, Doré V, Meyer L; ANRS IPERGAY Study Group. Post-exposure prophylaxis with doxycycline to prevent sexually transmitted infections in men who have sex with men: an open-label randomised substudy of the ANRS IPERGAY trial. Lancet Infect Dis. 2018 Mar;18(3):308-317.
[PubMed Abstract]

This next article is titled “Post-exposure prophylaxis with doxycycline to prevent sexually transmitted infections in men who have sex with men: An open-label randomized substudy of the ANRS IPERGAY trial,” which was published by Dr. Molina and colleagues and was an extension of the IPERGAY [On Demand Antiretroviral Pre-exposure Prophylaxis for HIV Infection in Men Who Have Sex With Men] trial in France, enrolling a cohort of MSM using PrEP for HIV prevention.

1. Randomized study of 230 MSM at high risk for HIV acquisition and were already on preexposure HIV prophylaxis.
2. Participants either took a single dose of doxycycline 200 mg daily [high dose] within 24 hours after sex or had no postexposure prophylaxis for STD.
3. They all remained on the preexposure HIV prophylaxis.
4. The primary endpoint was the occurrence of a first STD of gonorrhea, chlamydia, or syphilis in a 10-month follow-up period.

So, what did they find? The authors found that, overall, there was a 47% relative reduction in the risk of acquiring a new bacterial STD. So this is great! This is really promising! The occurrence of the first episode of chlamydia and syphilis were significantly lower in those taking the postexposure prophylaxis: the authors observed a 70% relative reduction in the risk of chlamydial infection and a 73% relative reduction in the risk of syphilis. However, not surprisingly, the time to the first episode of gonorrhea did not differ significantly between the two groups. The reason why this is not surprising is because of the widespread resistance of *Neisseria gonorrhoeae* to doxycycline in France.

I will note that it’s interesting that participants in this study used a median of 680 mg doxycycline/month. That’s not too much, right? There were some GI [gastrointestinal]-related issues, which is probably because of the 200 mg dose, but overall, it was pretty much tolerated. So the first question is, should we even try this? And then second, if one is going to use doxycycline for STD prevention, the question remains, is pre- or postexposure doxycycline better? At this point, I think we need more data to answer these questions.

[06:07] Paper #3

Spinelli MA, Scott HM, Vittinghoff E, Liu AY, Coleman K, Buchbinder SP. High interest in doxycycline for sexually transmitted infection postexposure prophylaxis in a multicity survey of men who have sex with men using a social networking application. Sex Transm Dis. 2019 Apr;46(4):e32-e34.
[PubMed Abstract]
So, I alluded to at the beginning that patients might be interested in STD prophylaxis, at least in my clinical experience. But is this really true? That brings me to our third article. The main point is that there is some data to suggest that patients would be interested in this type of method to protect them from STDs. This study was published by Dr. Matthew Spinelli and colleagues in April 2019 in *Sexually Transmitted Diseases* and is titled “High interest in doxycycline for sexually transmitted infection postexposure prophylaxis in a multicity survey of men who have sex with men using a social networking application.”

1. The study was an anonymous online survey of users of a gay social networking application in 6 US cities: Atlanta, Birmingham, Chicago, New York, San Francisco and Seattle.
2. The application already had 160,000 active users at the time of the study and the authors received about 1,300 respondents.
3. The median age of the participants was 34 years old, 96% were cis men, and the sample was racially, ethnically diverse.

What did they find? They found that 84% of participants—the majority of respondents—expressed interest in trying doxycycline postexposure prophylaxis for prevention of STDs. Interestingly, more than a third of the individuals interested in doxycycline postexposure prophylaxis had an STD in the last year. What this survey study shows us is that there is interest from patients in the community in taking doxycycline postexposure prophylaxis. Research into the study uptake, safety, efficacy, and long-term impact of this antibiotic could be an important area of further study, so stay tuned for more to come on this topic.

[08:05] Summary
Here's the thing. In a world where the clinical community is trying to implement careful antibiotic stewardship, long-term treatment with antibiotics can have some potential but significant consequences. For example, doxycycline has the potential to induce shifts in bacterial communities of the microbiome. It also has the potential to select for resistant strains of bacteria, and increase background resistance of *Neisseria gonorrhoeae* in a community. It's also possible that long-term doxycycline could enhance the development of drug resistance with common skin bacteria, for example, staph [staphylococcal] and strep [streptococcal]. Although personally, I think it would make your skin quite nice and free from acne. We use doxycycline a lot as clinicians—at least I do—sometimes for pneumonia, skin and soft tissue infections, patients who have allergies to other antibiotics, and some MRSA [Methicillin-resistant Staphylococcus aureus] infections.

Right now, doxycycline prophylaxis for STDs is not in any guidance for routine use, but I do look forward to seeing the outcomes of larger trials on this topic, as the articles mentioned do have some very promising results. If you're interested in hearing more or seeing the outcomes of larger trials, please visit ClinicalTrials.gov for the latest information on these trials.

To conclude, I'd like to summarize some key points from this session:

1. Doxycycline preexposure and postexposure prophylaxis are being assessed to reduce the incidence of STDs in the MSM community. Both of these approaches—both pre- and postexposure prophylaxis—have shown some promising preliminary results, specifically to reduce the incidence of chlamydia and syphilis.
2. Preliminary data have also shown that antibiotic prophylaxis for STDs is of interest to certain communities at risk of acquiring STDs.
3. The benefits of using doxycycline for STD prophylaxis need to be weighed against the concern for safety, the risk of acquired drug resistance, both for STDs as well as non-STD-causing bacteria, and I think we'll hear more about this topic in the near future.
4. Lastly, further research in this field is needed to determine the effectiveness of doxycycline for STD prophylaxis, and to sort out the most effective way to use it. I'm excited about this idea, preventing STDs with a pre- or postexposure medication, but I'm not yet ready to implement long term doxycycline for all my patients until we get more information. I do think that my patients are going to start asking more about this and I want to be prepared to convey what I can from the literature on this topic.

[10:42] Credits
This podcast is brought to you by the National STD Curriculum, the University of Washington STD Prevention Training Center, and is funded by a grant from the Centers for Disease Control and Prevention.

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