Literature Review

National STD Curriculum Podcast

Treatment of Rectal Chlamydia

September 15, 2020

Season 1, Episode 1

Chlamydia infection can be treated with either azithromycin or doxycycline. Increasing evidence supports the use of doxycycline over azithromycin for the treatment of rectal chlamydia infection. This podcast summarizes literature on this topic.

Topics:

- Chlamydia
- doxycycline
- azithromycin

Meena S. Ramchandani, MD, MPH
Associate Editor
Associate Professor of Medicine
Division of Allergy and Infectious Diseases
University of Washington

Disclosures

Disclosures for Meena S. Ramchandani, MD, MPH
Consulting Fee: Innoviva Specialty Therapeutics

References

Paper #1 **Paper #2** **Paper #3**

Transcript

Read along with the audio or jump to a particular chapter.

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 a 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.

[**00:22] Background:**
I'd like to focus this podcast on the topic of the treatment of rectal chlamydia infection. The reason being

there is some debate regarding whether azithromycin or doxycycline is the best antibiotic for treating rectal chlamydia. In the U.S., current guidelines recommend treating rectal chlamydia with either a single dose of azithromycin 1 g or doxycycline 100 mg twice a day for 7 days. Now, from a provider point of view, the single dose of azithromycin is attractive because the patient will be compliant; I'm sure it's also attractive from a patient point of view. But, there is increasing evidence that doxycycline might be better therapy for rectal chlamydia. Based on this evidence, I actually had changed my practice to treat all my patients with rectal chlamydia infections with doxycycline instead of azithromycin. Some guidelines, including the European and Australian guidelines, now recommend treating rectal chlamydia infection with 7 days of doxycycline as a first-line therapy. So, for this session, I'd like to delve into the literature published on this topic. It goes back a few years. Unfortunately, as of yet, there are no published randomized trials directly comparing the two treatments.

[**01:30] Paper #1:**

Khosropour CM, Dombrowski JC, Barbee LA, Manhart LE, Golden MR. Comparing azithromycin and doxycycline for the treatment of rectal chlamydial infection: a retrospective cohort study. Sex Transm Dis. 2014 [PubMed Abstract]
So starting chronologically in February 2014, there was a study published in *Sexually Transmitted Diseases* titled "Comparing azithromycin and doxycycline for the treatment of rectal chlamydial infection: A retrospective cohort study." This was published by Dr. Christine Khosropour and colleagues and took place at the STD clinic in Seattle, Washington. It was a retrospective cohort of men analyzed from 1993 to 2012 with rectal chlamydia infection.

1. They analyzed a large group of participants—they had 502 men that came back for repeat testing posttreatment and these patients were treated with either the azithromycin or the doxycycline: 81% of patients got azithromycin—so the majority of patients—and then a minority of patients (19%) got doxycycline.
2. The authors compared treatment outcomes at four repeat testing time intervals in order to maximize the number of follow-up tests included in the analysis.
3. And what they found is that 22% of the azithromycin-treated group and 8%—so, only 8%—in the doxycycline-treated group had evidence of persistent or recurrent infection. And this was significant with a p-value of .002.
4. They also adjusted for confounders and they found that treatment with azithromycin was significantly associated with a 5-fold higher risk of persistent or recurrent infection—you can't really tell the difference—at 14 to 90 days after treatment.

So, this study is one of the largest there are out there looking at rectal chlamydia treatment in men, and they found at each repeat test interval, persistent or recurrent infection was higher among men treated with azithromycin compared to those treated with doxycycline. The association was observed when testing was done using culture or a nucleic acid amplification test (or NAAT) for rectal specimen, and they were looking at patients over a number of years. The findings just add to this growing body of evidence suggesting that azithromycin may be inferior to doxycycline for the treatment of rectal chlamydia.

[**03:39] Paper #2:**

Li B, Hocking JS, Bi P, Bell C, Fairley CK. The efficacy of azithromycin and doxycycline treatment for rectal chlamydial infection: a retrospective cohort study in South Australia. Intern Med J. 2018 [PubMed Abstract]
So this takes me to my next article on this topic, and this was published in June of 2017. And this was a manuscript in *Internal Medicine Journal* and it was titled: "The efficacy of azithromycin and doxycycline treatment for rectal chlamydial infection: A retrospective cohort study in South Australia." And this was published by Dr. Bin Li and colleagues.

1. So this was a retrospective analysis of patients, and they included both men and women with rectal

chlamydia infections between 2009 to 2015 at a sexual health clinic.

2. They had 526 patients with rectal chlamydia. They had the majority of patients treated with doxycycline, so 80% of patients got doxycycline as treatment, and 18% of patients got azithromycin. Of note, patients were treated with 10 days of doxycycline, so not the 7 days that's recommended by the CDC guidelines in the U.S. Also, I want to point out that during this period, the recommended treatment for rectal chlamydia infection in Australia—so the guidelines changed from azithromycin to doxycycline being the first-line therapy, so that might be why the majority of patients were treated with doxycycline in this group. And this is a nice contrast to the paper that I just discussed by Dr. Christine Khosropour and colleagues in which the majority of patients in that study were treated with azithromycin.

   So, getting back to the manuscript by Dr. Bin Li.
3. The group found that 204 patients returned for repeat testing—so these were the patients that they analyzed—and they found those treated with azithromycin were at higher risk of repeat rectal NAAT positivity than those patients treated with doxycycline. The repeat rectal chlamydia test positivity was 19% in the azithromycin-treated patients compared to only 6% in the doxycycline-treated patients. See, when I see that data, I think for my patient, I'm going to treat that patient with doxycycline, whoever has rectal chlamydia infection.

   It's just another study that suggests doxycycline is more effective than azithromycin, specifically for rectal chlamydia infections. The authors found that treatment with azithromycin was significantly associated with almost a 3-fold higher risk of repeat rectal chlamydia infection 14 to180 days after treatment.

[**06:01] Paper #3:**

Dukers-Muijrers N, Wolffs PF, De Vries H, Götz HM, Heijman T, Bruisten S, Eppings L, Hogewoning A, Steenbakkers M, Lucchesi M, Schim van der Loeff MF, Hoebe C. Treatment effectiveness of azithromycin and doxycycline in uncomplicated rectal and vaginal chlamydia trachomatis infections in women: A multicenter observational study. Clin Infect Dis 2019.
[PubMed Abstract]
Now in most of the studies on rectal chlamydia, the focus has been on men, and specifically MSM [men who have sex with men]. Women are largely underrepresented. But, a recent article published in *Clinical Infectious Diseases*, January 2019, reported on rectal chlamydia treatment in women, and it is titled "Treatment effectiveness of azithromycin and doxycycline in uncomplicated rectal and vaginal *chlamydia trachomatis* infections in women: A multicenter observational study," and this was written by Dr. Nicole Dukers-Muijrers and colleagues.

1. This was part of a prospective multicenter cohort study in the Netherlands evaluating patients at three STD clinics.
2. As I mentioned before, it's unique in that it included women, for which the data on rectal chlamydia infections is scarce, and it was quite a large study. They had 416 women diagnosed with rectal and/or vaginal chlamydia that were analyzed. They assessed the effectiveness of doxycycline 100 mg twice a day—and they used 7 days—or azithromycin 1 gram for one dose for the treatment of either rectal and/or vaginal chlamydia infections. Microbiological cure was defined by a negative NAAT at 4 weeks posttreatment.
3. They found, of their cohort, 77% of the women had both rectal and vaginal chlamydia infection, 5% had rectal chlamydia infection alone, and 18% had vaginal chlamydia infection alone. So the majority of the women had both rectal and vaginal chlamydia infection.
4. When they analyzed the data they found that for rectal chlamydia infections the microbiological cure was quite different depending on the antibiotic treatment. They found a 96% cure rate for women treated with doxycycline versus only 79% for those women treated with azithromycin for rectal chlamydia.
5. Now, for vaginal chlamydia infections, microbiological cure was similar with the two treatments—95%

of patients were cured with doxycycline and 94% of patients were cured with azithromycin, so not much of a difference.

Overall, on multivariate analysis, the authors found the odds for not reaching microbiological cure was 9.4 times higher for those treated with azithromycin than for those treated with doxycycline for rectal chlamydia infections. And, like I said before, you can't really tell if a patient has been reinfected, versus a persistent infection.

[**08:40] Summary:**
To conclude, I'd like to summarize some key points from this session:

1. There is a limited, but growing body of evidence that azithromycin might be inferior to doxycycline for the treatment of rectal chlamydia, and that's for both men and women.
2. It's not clear why azithromycin is less effective for rectal chlamydia infections—it may be related to the bioavailability of azithromycin in rectal tissue, it could be related to the organism load in the rectum, but I think the reasons remain to be determined.
3. So until we have more data in the U.S., both azithromycin and doxycycline can be used for treating rectal chlamydia infections.
4. But, I will say that my practice has changed so that for my patients with rectal chlamydia infection, I'll treat with doxycycline over azithromycin.

Stay tuned for more information on this topic as randomized control trials are currently being done in the U.S. and other countries to help answer some of the questions discussed in this podcast.

[**09:39] Credits:**
This podcast is brought to you by the National STD Curriculum, the STD Prevention Training Center at the University of Washington, and is funded by a grant from the Centers for Disease Control and Prevention.

References for this podcast can be found on our web site, the National STD Curriculum at www.std.uw.edu.