

Hot Topic

National STD Curriculum Podcast

New Medications for Gonorrhea Treatment

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Season 1, Episode 2

Gonorrhea has developed resistance to many antibiotics available and few options remain to treat this STI [sexually transmitted infection]. This podcast episode summarizes three articles recently published on new treatments for gonorrhea, specifically looking at gentamicin, delafloxacin, and zoliflodacin.

Topics:

- Antibiotic Resistance
- Gonorrhea
- gentamicin
- delafloxacin
- zoliflodacin

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[Disclosures](#)

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[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

This first topic keeps coming up—and that is the concern for gonorrhea resistance in the community, and what we are going to do as health care providers to treat this infection if we have no antibiotics left. Gonorrhea has progressively developed resistance to the antibiotic drugs we have available to treat the infection. Our clinic in Seattle is a GISP site (the CDC-funded gonococcal isolate surveillance project site) and I'm always worried that we're going to get some isolate that is resistant to both ceftriaxone and azithromycin and, as health care providers, we're going to have to figure out how to treat this organism and take care of the patient. Thankfully, we have investigators that are studying alternatives to ceftriaxone. So along these lines, I've chosen to review three relatively recently published articles that have evaluated alternatives to ceftriaxone for the treatment of gonorrhea. Why is this important? Well, for one thing, we may need the medications in the future for treating drug-resistant strains; and second, we need better options for those persons with a major allergy to ceftriaxone. The three drugs I will be discussing are gentamicin, delafloxacin, and the investigational drug zoliflodacin.

[01:38] Paper #1

Ross JDC, Brittain C, Cole M, et al. Gentamicin compared with ceftriaxone for the treatment of gonorrhoea (G-ToG): a randomised non-inferiority trial. *Lancet*. 2019;393:2511-20.

[\[PubMed Abstract\]](#)

The first article—this one was published in *Lancet* in May 2019—was titled “Gentamicin compared with ceftriaxone for the treatment of gonorrhea: A randomized non-inferiority trial”. The study was led by Dr. Jonathan Ross and colleagues and gives us a glimpse into whether gentamicin can be used instead of ceftriaxone for gonorrhea treatment. The end result is that it shouldn't be used as first-line therapy.

Key features of the study

1. First of all, it was randomized.
2. They evaluated the effectiveness of one dose of intramuscular gentamicin compared with intramuscular ceftriaxone; all patients received oral azithromycin as part of their care and the treatment regimen.
3. The authors found that 98% of participants in the ceftriaxone group and 94% of persons in the gentamicin group had clearance of genital infection.
4. They found that the clearance of infection with gentamycin was markedly lower for pharyngeal and rectal gonorrhea than with ceftriaxone. For example, only 80% of those with pharyngeal gonorrhea and 90% of those with rectal gonorrhea cleared their infection with gentamicin.

So what does this tell us? It tells us that the study unfortunately failed to show that gentamicin was noninferior for the treatment of uncomplicated gonorrhea compared to ceftriaxone.

I like this study because data on the efficacy of gentamicin for the treatment of gonorrhea is scarce in the literature and we just need more data. The study had the advantage of using nucleic acid amplification testing, which is a much more sensitive test than culture to monitor infection or cure. And lastly, this study evaluated the effect of this antibiotic to cure extragenital infections in a large number of individuals. This is important because a lot of antibiotics just don't treat *Neisseria gonorrhoea* in the oropharynx very well.

As a clinician, I wouldn't use gentamicin as first-line therapy for gonorrhea, especially for pharyngeal infection. Now, if a patient had a major allergy to ceftriaxone, then gentamycin can be used. We just used this in the clinic the other day for a patient who reported anaphylaxis reaction to ceftriaxone. The [2015 STD](#)

[Treatment Guidelines](#) recommend that a patient with gonorrhea and a major allergy to ceftriaxone should receive gentamicin 240 mg intramuscular, as well as azithromycin 2 grams orally. Of note, this is a higher dose of azithromycin but if a patient has gonococcal pharyngeal infection and receives this alternative regimen, I'd recommend getting a test-of-cure, as recommended by the guidelines.

[04:25] Paper #2

Hook EW 3rd, Golden MR, Taylor SN, et al. Efficacy and Safety of Single-Dose Oral Delafloxacin Compared With Intramuscular Ceftriaxone for Uncomplicated Gonorrhea Treatment: An Open-Label, Noninferiority, Phase 3, Multicenter, Randomized Study. *Sex Transm Dis*. 2019 May;46:279-286.

[PubMed Abstract]

The next article is relevant to the first one in that it's also looking for an alternative treatment for gonorrhea. This article was published in *Sexually Transmitted Diseases*, also in May 2019, by Dr. Ned Hook and colleagues and is titled "Efficacy and safety of oral delafloxacin compared with ceftriaxone for uncomplicated gonorrhea treatment: An open-label, noninferiority, phase 3, multicenter, randomized study." So one question is: What is delafloxacin and why would a fluoroquinolone work against gonorrhea? We don't really use fluoroquinolones that much anymore given increasing resistance, and the CDC no longer recommends this class of drugs as therapy given circulating resistant strains to (for example) ciprofloxacin. The difference is that delafloxacin is a novel fluoroquinolone and it has some promising activity against gonorrhea, even for those strains with ciprofloxacin resistance.

Key features of this study

1. Randomized, open-label and at 25 centers.
2. Participants received either a single dose of 900 mg delafloxacin or intramuscular ceftriaxone for *Neisseria gonorrhoeae* urogenital infection.
3. They also used nucleic acid amplification testing—I'm going to start saying NAAT—to demonstrate microbiological cure and evaluated extragenital sites, which are both important when looking at the efficacy of an antibiotic for gonorrhea.

What they found is that, unfortunately, the urogenital cure rates for delafloxacin were just not that great. Only 85% of persons cured infection with delafloxacin, compared to a the 91% cure rate seen in the ceftriaxone group.

Not surprisingly, treatment failures were higher for those with *Neisseria gonorrhoeae* isolates with higher delafloxacin MIC [minimum inhibitory concentration] values. These particular isolates were found more often in MSM [men who have sex with men] than compared to other subgroups.

I do want to point out a nice [editorial by Dr. Hunter Handsfield and Dr. Jonathan Zenilman](#) in the same journal [*Sexually Transmitted Diseases*], and I'd encourage you to read this if you're interested.

So, sorry clinicians, delafloxacin is not a promising agent to use in clinical practice right now. This further confirms how difficult it is to treat gonococcal infections due to antimicrobial resistance and the characteristics of this organism. We just need better or new antimicrobial therapy, as well as innovative ways to prevent the spread of disease.

[06:56] Paper #3

Taylor SN, Marrazzo J, Batteiger BE, et al. Single-Dose Zoliflodacin (ETX0914) for Treatment of Urogenital Gonorrhea. *N Engl J Med*. 2018 Nov 8;379:1835-1845.

[PubMed Abstract]

So last I'd like to take a look at this study, which was published in November 2018 in the *New England Journal of Medicine* by Dr. Stephanie Taylor and colleagues, titled "Single-dose zoliflodacin for treatment of urogenital gonorrhea." So what is zoliflodacin? It's a new antibiotic that inhibits the formation of fused circular DNA

required for microbial biosynthesis. Well, you don't have to remember details of the mechanism, but what is important, as a clinician, is that this antibiotic has been shown to be active against both chlamydia as well as *Mycoplasma genitalium*. It's the trifecta of an antibiotic. What's also great is that it's an oral drug and can be given as a single dose.

Key features of this study

1. Randomized but open-label; they had three groups of participants.
2. Participants received either a dose of 2 grams of zoliflodacin, 3 grams of zoliflodacin (remember, this is an oral medication), or intramuscular ceftriaxone for urogenital gonorrhea. Of note, they also used 500 mg of ceftriaxone, which is higher than what we are currently using in the U.S., and that's because they wanted to meet the requirements of both the FDA [Food and Drug Administration], as well as the European Medicines Agency.
3. The good news is that this antibiotic did really well for urogenital gonorrhea. With regards to microbiological cure at urogenital sites, this was achieved in 96% of those participants receiving 2 grams of zoliflodacin, 96% in those receiving 3 grams, compared to the 100% who received ceftriaxone.
4. All of the rectal infections were cured in all three groups, but as a side note, there weren't that many rectal infections overall.
5. The unfortunate news is that similar to other antibiotics, this is not a great drug for pharyngeal gonorrhea. Only 50% of participants receiving the 2 grams of zoliflodacin had microbiological cure. It is interesting that the higher dose of zoliflodacin at 3 grams achieved 82% microbiological cure, but this just wasn't as good as the ceftriaxone group, which had 100% cure rate for those with pharyngeal gonorrhea (this was only 4 participants, so the numbers were small).

Overall, zoliflodacin seems to be effective in treating urogenital and rectal gonorrhea. With regards to pharyngeal infection, these antibiotics seem to have poor drug penetration into the pharyngeal tissue.

There is an ongoing multicenter, randomized, noninferiority study comparing zoliflodacin and ceftriaxone/azithromycin for treatment of uncomplicated gonorrhea. Check out [ClinicalTrials.gov](https://clinicaltrials.gov) to see if there is a site near you and you're interested in learning more.

[09:39] Summary

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

1. Gentamicin is not appropriate as first-line treatment of *Neisseria gonorrhoea*. The preferred treatment for gonorrhea includes ceftriaxone and azithromycin, especially for extragenital infections. However, gentamicin is a useful alternative in those patients with a severe allergy to ceftriaxone.
2. Delafloxacin is a fluoroquinolone antibiotic and it is not a reliable treatment for urogenital gonorrhea.
3. Zoliflodacin, on the other hand, is a new antibiotic and seems to have high efficacy for urogenital and rectal gonorrhea, but not pharyngeal infection. It's not yet available, but stay tuned for future studies on this drug.

[10:26] Credits

This podcast is brought to you by the National STD Curriculum, the University of Washington STD Prevention Center, and is funded by a grant from the Centers for Disease Control and Prevention

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

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