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Is It Time to Reconsider Azithromycin Therapy for Urogenital Chlamydia Infections?

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Every year or so, I find an article that I can use to teach almost all aspects of evidence-based medicine; this is my article for 2016. I could spend all 4 blog posts this month pointing out key features of this study, but instead I'll contain my enthusiasm and mention 3 take-home points.


PICO Question: Among youth aged 12-21 years with urogenital chlamydia infection, is treatment with oral azithromycin associated with more treatment failures compared to treatment with oral doxycycline?

Question type: Intervention

Study design: Randomized

This was a randomized, open label (i.e. not blinded), noninferiority trial of single dose azithromycin compared to 7 days of doxycycline for treatment of urogenital chlamydia infection in adolescents. Of 155 participants in each group, the investigators found 5 treatment failures in the azithromycin group and none in the doxycycline group. These results, based on the prespecified statistical measures of the trial, meant that azithromycin therapy could not be considered noninferior to the doxycycline regimen. Stated differently, doxycycline might be better than azithromycin as treatment for this condition.

But here's the real kicker: the study was carried out in residential juvenile correctional facilities, and thus the study participants took their medication under direct staff supervision at the facility. Also, sexual intercourse was theoretically prohibited at the sites, limiting the chances for reinfection. (The investigators did find evidence that sexual contact likely did occur, but perhaps less likely than in a non-captive study group.)

The first element to notice is the concept of a noninferiority trial. Most clinical trials are superiority trials, with enough patients to find a difference in treatment regimens if such a difference exists. However, sometimes it's difficult to mount a trial with sufficient patients, and a noninferiority trial can be accomplished with fewer subjects and, if successful, can state that treatment A is not significantly inferior to treatment B, with the margin of inferiority defined prior to starting the study. Of course, if a larger study is performed for the same question, the same results might end up showing statistically significant inferiority even with that same margin. I've talked about noninferiority trials previously if you want a refresher.

The second point I wanted to mention was the generalizability of research studies. If we want to apply study results to our own clinical practices, we need to know if the study conditions (patient population, setting, ease of complying with treatment regimens, etc.) are transferable to our practice. Clearly, that's a big deal with this study, unless your medical practice is set in a custodial institution. Administering a single dose of azithromycin in your clinic is a lot better from a compliance perspective than is asking your patient to complete a 7-day course of twice daily medication at home. So, while azithromycin was noninferior (and who knows, maybe truly worse)
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than 7 days of doxycycline, we would all bet that the small difference might disappear in a more routine clinical setting where patients might not take all their doxycycline.

One final note pertains to research ethics. The choice of an incarcerated patient population for research raises many ethical concerns, most specifically the principal of autonomy (aka respect for persons). This principal is 1 of the 3 cornerstones of the Belmont Report, the others being beneficence and justice. Offering prisoners opportunities to participate in research may involve subtle coercion that isn't present in other settings. Of course, the authors of this study complied with rules governing research in prison-like conditions.

I've only mentioned 3 topics so far, and I'm just getting warmed up about this study. Take time and read it, see what questions occur to you!

Further Reading

- Chlamydia Infections in Children and Adolescents
- Grand Rounds on Facebook
- AAP Journals in Twitter