

BRIEF REPORT

Infectious Disease

Adherence to doxycycline for uncomplicated genitourinary chlamydia: A prospective observational study

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Abstract

Objectives: Since 2020, the Center for Disease Control and Prevention (CDC) no longer recommends single-dose azithromycin as first-line therapy for uncomplicated genitourinary chlamydia, advising instead a 7-day course of doxycycline. Our study investigates self-reported adherence to the new regimen, reasons for nonadherence, and the impact of dispensing the regimen on-site compared to prescribing it.

Methods: We performed a prospective observational study of adult patients treated for suspected or laboratory-confirmed uncomplicated genitourinary chlamydia at three urban emergency departments (EDs), where patients receive a prescription for doxycycline, and in a sexually transmitted infection (STI) clinic, where the 14 doxycycline pills are dispensed on-site. Clinical data were extracted from electronic medical records and patients were interviewed regarding adherence via telephone 2–4 weeks after their index visit.

Results: We enrolled 127 STI clinics and 201 ED patients. Therapeutic adherence was reported by 85% of STI clinic patients and 77% of ED patients. In the ED setting, younger age and female sex were associated with nonadherence, with only 67% of female patients reporting adherence. Reported reasons for nonadherence included medication adverse effects, financial and transportation barriers, skepticism of the need for therapy, and misunderstanding of discharge instructions, among others.

Conclusion: A considerable portion of patients treated for uncomplicated genitourinary chlamydia in urban EDs and STI Clinics report nonadherence to the 7-day doxycycline regimen. The CDC recommendation to consider azithromycin when nonadherence is a “substantial concern” should be applied broadly in these settings by routinely discussing barriers to adherence when selecting the optimal antimicrobial regimen. The benefit of dispensing the doxycycline regimen on-site compared to prescribing it could not be determined given differences in baseline characteristics between the two groups.

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1 | INTRODUCTION

1.1 | Background

In 2020, the Center for Disease Control (CDC) updated its treatment guidelines for uncomplicated genitourinary chlamydia, replacing the single oral dose of azithromycin with a 7-day course of twicedaily oral doxycycline.^{1,2} Citing concerns for bacterial resistance and decreased effectiveness compared to doxycycline, single-dose azithromycin was relegated to use in pregnant patients and those in whom nonadherence is a “substantial concern.” However, available evidence on nonadherence is limited to studies that evaluated longer regimens or specific populations.^{3–6}

1.2 | Importance

Chlamydia trachomatis is the most frequently reported bacterial sexually transmitted infection (STI) in the United States.² Failure to treat chlamydial infections can lead to increased transmission, pelvic inflammatory disease, ectopic pregnancy, and infertility.² Increased incidence of azithromycin resistance and marginally greater efficacy justify the CDC’s recommendation of doxycycline over azithromycin as first-line therapy. However, the risk of nonadherence to the weeklong regimen remains unknown, hindering clinicians’ ability to choose the optimal antibiotic regimen.

1.3 | Goals of this investigation

We aimed to measure adherence in adult patients treated with 7 days of doxycycline for uncomplicated genitourinary chlamydia in urban EDs and an STI clinic. We also sought to identify factors associated with nonadherence, and to measure the impact of dispensing the regimen on-site compared to prescribing it.

2 | MATERIALS AND METHODS

2.1 | Study design and settings

This was a prospective observational study of adult patients treated for uncomplicated genitourinary chlamydia at three urban, academic emergency departments, where patients receive a prescription for doxycycline, and in an urban, public health STI clinic, where the 14 doxycycline pills are dispensed on-site. We included patients treated empirically for suspected chlamydia as well as those treated for laboratory-confirmed infections at the time of their index visit.

Enrollment started in October 2021 and continued intermittently until March 2023 based on the availability of investigators.

Our study was approved by the Wayne State University School of Medicine Institutional Review Board. It adheres to the Strengthen-

The Bottom Line

The 2021 guidelines from the Center for Disease Control and Prevention recommend a 7-day course of doxycycline for uncomplicated genitourinary chlamydia. While single-dose azithromycin is still endorsed for patients in whom nonadherence is a “substantial concern,” there is limited evidence for clinicians to make this determination. In this study, 23% of emergency department (ED) patients and 15% of sexually transmitted infection (STI) clinic patients reported nonadherence to the week-long doxycycline regimen. This study’s findings of nonadherence to 7-day treatment suggest single-dose therapy should be routinely considered for patients with uncomplicated genitourinary chlamydia treated in these healthcare settings.

ing the Reporting of Observational Studies in Epidemiology (STROBE) guidelines.

2.2 | Selection of participants

Adult patients treated for suspected or confirmed uncomplicated genitourinary chlamydia with a 7-day course of doxycycline were identified via electronic medical records. Patients instructed by their clinicians not to complete the regimen were excluded. Patients with anorectal or complicated infections were excluded. A convenience sample was selected based on the availability of the investigators to contact all patients seen each week at each site.

2.3 | Data collection

Demographic and clinical data were collected from the electronic medical record. Eligible patients were contacted via telephone 2–4 weeks after their index visit to obtain informed consent and complete an interview. Up to three attempts on different days were made to contact each patient. Whenever possible, a voice message was left asking the patient to return the call. Figure 1 summarizes patient selection and enrollment.

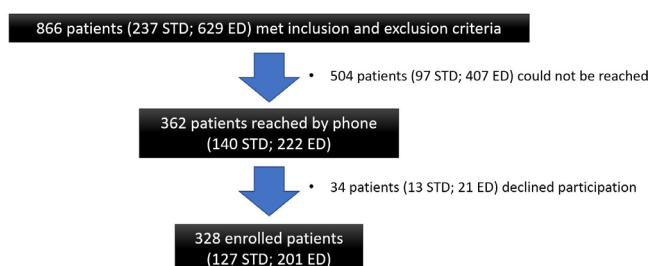


FIGURE 1 Patient selection and enrollment pathway.

TABLE 1 Clinical characteristics and results of 328 patients.

Variable	Patients, No. (%)		
	STI clinic	EDs	Total
Age (years)			
18-25	24 (19)	62 (31)	86 (26)
26-35	50 (39)	68 (34)	118 (36)
36-45	28 (22)	43 (21)	71 (22)
>45	25 (20)	28 (14)	53 (16)
Sex			
F	13 (10)	101 (50)	114 (35)
M	114 (90)	100 (50)	214 (65)
Diagnosis			
Suspected	117 (92)	198 (99)	315 (96)
Confirmed	10 (8)	3 (1)	13 (4)
Pills taken			
All Some	108 (85)	154 (77)	262 (80)
None	18 (14)	19 (9)	37 (11)
	1 (1)	28 (14)	29 (9)
Prescription filled			
Yes	N/A	174 (87)	N/A
No	N/A	27 (13)	N/A
Reason for nonadherence			
Adverse Effect	3 (2)	7 (3)	10 (3)
Financial	0 (0)	6 (3)	6 (2)
Transportation	0 (0)	3 (1)	3 (1)
Felt Unneeded	2 (2)	9 (4)	11 (3)
Misunderstanding	1 (1)	3 (1)	4 (1)
Other	13 (10)	19 (9)	32 (10)
Total	127	201	328

Abbreviations: ED, emergency department; STI, sexually transmitted infection.

2.4 | Outcome measures

Our primary outcome was adherence to therapy, defined as completion of the 7-day doxycycline regimen. Additional outcomes included prescription filling and reported reasons for nonadherence, the latter of which were subsequently categorized independently by the authors into one of the following groups: medication adverse effects, financial barriers, lack of transportation, skepticism of the need for therapy, and misunderstanding of discharge instructions, among others. Included in the category of other reasons were forgetting to fill the prescription or take the pills, being too busy, losing the prescription or pills and no reason provided.

2.5 | Statistical analysis

Descriptive statistical analysis was performed using IBM SPSS Statistics (version 26) and MedCalc.⁷ We have included 95% confidence

TABLE 2 Examples of patient reported reasons for nonadherence.

I did not feel I needed all of them. It was just precautionary.
My symptoms resolved.
I dropped off the prescription but I had no time to pick it up.
I received a shot in the ER and did not feel I needed the pills.
I lost the prescription.
I lost the pills.
I forgot to fill the prescription.
They were not helping my abdominal pain.
I did not think I had an STI.
I was trying to get my insurance sorted out before trying to fill it due to concerns of cost.
They made me feel sick so I was taking one a day.
I did not realize I was supposed to. I thought the medications I got in the ED were it.
They made me feel nauseous.
I felt different while taking them and thought I was having a reaction to the medication.
The pharmacy did not take my insurance.
I felt the medication I received in the ED fixed my problem.
The prescription was not signed and they would not fill it.
I had no money to buy the medications.
I stopped because I was vomiting.
I started drinking and I thought it would not work if I was drinking, so I stopped.
I stopped because of GI upset.
I was only taking one pill daily because I was too busy with work.
I did not have food to take with pills.
I forgot. I have too many different medications.
I left the medications at home and I was out of town.
My symptoms got better, so I did not finish the course.

Abbreviations: ED, emergency department; STI, sexually transmitted infection.

intervals so the reader can understand the possible precision of estimates but, since this was not a randomized experimental design, we discourage any assessment of statistical significance.

3 | RESULTS

3.1 | Characteristics of study groups

A total of 866 patients met inclusion and exclusion criteria, of whom 328 were enrolled in the study: 201 were seen in the EDs and 127 at the STI clinic.

There were important differences in baseline characteristics between the two groups (Table 1). Notably, the patients seen in the ED setting were equally male and female, while the patients treated in

TABLE 3 Adherence by variable and by setting.

Variable	STI clinic				EDs			
	Adherent	Total	%	95% CI	Adherent	Total	%	95% CI
Age								
18–25	20	24	83	70–100	42	62	68	57–80
26–35	43	50	86	77–96	48	68	71	60–82
36–45	24	28	86	74–100	37	43	86	76–97
>45	21	25	84	71–100	27	28	96	90–100
Sex								
Female	12	13	92	79–100	68	101	67	59–77
Male	96	114	84	78–91	86	100	86	79–93
Diagnosis								
Suspected	99	117	85	78–91	151	198	76	70–82
Confirmed	9	10	90	73–100	3	3	100	29–100
Prescription filled								
Yes	N/A	N/A	N/A	N/A	154	174	89	84–93
Total	108	127	85	79–91	154	201	77	71–83

Abbreviations: ED, emergency department; GI, Gastrointestinal; N/A, not applicable; STI, sexually transmitted infection.

the STI clinic were overwhelmingly male (90%); patients from the ED group were younger, with a higher proportion in the 18–25 years old bracket (31% vs. 19%); and lastly, only 1% of ED patients were treated for a laboratory-confirmed infection at the time of their index visit versus 8% of the STI clinic patients.

3.2 | Main results

Table 1 summarizes our findings. Adherence to therapy, defined as the self-reported completion of the 7-day course of doxycycline, was 85% in the STI clinic group (95% confidence interval [CI] 79%–91%) and 77% in the ED group (95% CI 71%–83%). Only one (1%) STI clinic patient reported taking none of the pills, whereas 28 (14%) in the ED group did.

Notable examples of reported reasons for nonadherence are presented in Table 2. Financial and transportation barriers were only reported by ED patients (nine; 4.5% of all ED patients and 19% of all nonadherent ED patients), suggesting that providing pills rather than a prescription could help bridge this gap in adherence. Compared to STI clinic patients, a higher proportion of ED patients did not feel doxycycline therapy was indicated (5.0% vs. 1.6%). Adverse effects as the reason for nonadherence were reported by 1.6% and 3.5% of ED and STI clinic patients, respectively.

We analyzed the adherence of each group by variable (Table 3). In ED patients, adherence increased with age, with the youngest subset at 68% (95% CI 57%–80%) and the oldest at 96% (95% CI 90%–100%). Age was not a statistically significant factor in STI clinic patients. Male ED patients reported higher adherence (86%; 95% CI 79%–93%) than female patients (67%; 95% CI 59%–77%). Sex was not a statistically significant factor in STI clinic patients. While only 87% of ED patients

self-reported filling their prescriptions, adherence in this subset was significantly higher than in the ED group as a whole (89% [95% CI 84%–93%] vs. 77% [71%–83%]).

Determining the benefit of dispensing the medication on-site instead of prescribing it was not possible given the differences in baseline patient characteristics between the two settings.

4 | LIMITATIONS

Our study has several limitations. First, it was conducted in a single urban environment and may therefore not be generalizable. Second, we enrolled a convenience sample of patients based on availability of investigators; however, we do not have reason to believe this would alter the results. Third, of the 866 patients that met inclusion and exclusion criteria, we were unable to reach 504 (58%) and an additional 34 (4%) declined participation. There was a smaller percentage of unreachable patients in the STI clinic group (45%) than the ED group (66%). Lastly, there is evidence that self-reported medication adherence overestimates true adherence.^{8,9}

5 | DISCUSSION

In this study, 23% of ED patients and 15% of STI clinic patients did not adhere to the CDC-recommended 7-day doxycycline regimen for chlamydia. Factors associated with nonadherence in the ED setting include younger age and female sex. ED patients who filled their prescriptions reported higher adherence than STI clinic patients who received the doxycycline pills on-site, suggesting that patients who are motivated and able to fill their prescriptions are also highly driven to adhere to therapy.

To our knowledge, this is the first study that evaluates adherence to the new 7-day doxycycline regimen for uncomplicated chlamydia recommended by the CDC. Additionally, we studied undifferentiated ED and STI clinic adult populations. By demonstrating high rates of nonadherence in both settings, our study supports the CDC recommendation to consider single-dose azithromycin for patients in whom adherence is a “substantial concern,” highlighting the importance of selecting the optimal agent by weighing the risks of azithromycin, namely, bacterial resistance and lower effectiveness, against the risk of nonadherence to a 7-day course of doxycycline, even when patients are provided with pills instead of a prescription. By quantifying this risk and identifying associated factors, our findings can guide clinicians and their patients in shared decision-making.

The impact of dispensing pills rather than prescriptions could not be determined given the important differences in baseline characteristics between the two groups.

Future research should measure objective adherence and study broader patient populations, including those seen in primary care clinics and in rural and community settings. Clinical trials are likely needed to determine the impact in each setting of dispensing the regimen on-site rather than prescribing it.

Lastly, both groups showed a trend toward higher adherence in patients treated for a confirmed infection, suggesting that accurate point-of-care testing for gonorrhea and chlamydia could improve adherence in positive cases, in addition to decreasing unnecessary antibiotic use. The FDA recently approved the first of such tests.¹⁰

AUTHOR CONTRIBUTIONS

Dr. Ridelman conceived the study. All authors contributed substantially to the design of the study methodology, patient enrollment, and data analysis. All authors drafted the manuscript and contributed substantially to its revision. Dr. Ridelman takes responsibility for the paper as a whole.

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