Evaluation of Bacteriuria Treatment and Follow-up Initiated in the Emergency Department at a Veterans Affairs Hospital

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Abstract

Background: This study aims to evaluate the treatment and follow-up of bacteriuria in the emergency department (ED). **Objective:** The primary objective was to determine the frequency of patients discharged from the ED with antibiotics for symptomatic and asymptomatic bacteriuria, and the secondary objectives were to determine the frequency of patients receiving postdischarge antibiotic interventions and antibiotic-related adverse drug reactions (ADRs). **Methods:** This retrospective study evaluated patients with ED urine cultures sent between October 1, 2015, and November 24, 2015. Patients with indwelling catheters, concurrent antibiotics, and admission for inpatient care were excluded. *T* tests and contingency tables were applied in SAS; *P* < .05 was considered significant. **Results:** Of 429 unique patients with urine cultures drawn in the ED, 13.1% (*n* = 56) received treatment for a bacteriuria. The majority of patients discharged from the ED with antibiotics had urinary tract infection (UTI) symptoms documented in the medical record (76.8%; *n* = 43). Of those patients who required postdischarge interventions, 4 out of 13 had appropriate antibiotic adjustments based on culture and sensitivity results at follow-up. In a subset of patients with inappropriately ordered urine cultures (no UTI symptoms documented or antibiotic prescribed), a higher percentage of patients had normal urinalyses (UA) compared to abnormal UAs (83.3% vs 10.4%, *P* = .0008). No significant ADRs were identified. **Conclusions:** The majority of patients treated for bacteriuria in the ED had documented symptoms consistent with UTIs and appropriate empiric antibiotics. However, incorporating antimicrobial stewardship activities in the ED targeting unnecessary urine cultures and assuring postdischarge follow-up if treatment modification is needed based on culture results can improve antibiotic prescribing.

Keywords

asymptomatic bacteriuria, urinary tract infection, emergency department, antimicrobial stewardship

Introduction

The Infectious Diseases Society of America (IDSA) has published guidelines with recommendations for diagnosis and treatment of asymptomatic bacteriuria (ASB).¹ In the absence of dysuria, urinary urgency, suprapubic pain, or other signs or symptoms of infection, antimicrobial treatment following a positive urine screen is not recommended, except in pregnant women or patients scheduled for certain genitourinary procedures.^{1,2} Specifically in men, ASB is uncommon in the young and healthy, while the incidence is approximately 10% in men age >80 years.³

Despite these treatment guidelines, a number of studies assessing clinician adherence to guideline recommendations have shown rates of appropriate prescribing for bacteriuria in only 29% to 38% of outpatient cases.^{4–6} Avoiding inappropriate treatment of ASB can reduce adverse outcomes including antimicrobial resistance, adverse drug reactions (ADRs), and increased cost.¹

Antimicrobial stewardship programs (ASPs) are one of the tools recommended by the Centers for Disease Control and Prevention to help stem the increasing threat of antimicrobial resistance.⁷ However, while ASPs are effective tools, they tend to be better established in acute care compared to the outpatient setting. The emergency department (ED) represents a unique setting where ASPs are less commonly utilized.^{8,9} Currently, limited literature assessing antimicrobial stewardship in this setting exists. Some of the challenges with implementation of ASPs in EDs include rapid patient turnover, diverse patient needs, high number

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of providers, limited resources, and high staff turnover rates.¹⁰ Patients with a suspected urinary tract infection (UTI) can be discharged from the ED with unnecessary or inappropriate antibiotic therapy or lack of urine culture follow-up.¹¹ Thus, the purpose of this study was to evaluate the treatment and follow-up of urine cultures in the ED at a VA hospital to determine if improvements could be made with antibiotic prescribing.

Methods

Study Design and Setting

This retrospective, observational cohort study evaluated patients with urine cultures sent from the ED for analysis at a 471-bed tertiary care VA hospital that serves over 57 000 veterans with 23 000 ED visits annually. At the time of this study, there was no ED pharmacist or ED-specific antimicrobial stewardship resources or tools, institution-specific empiric UTI prescribing guideline or policies for ordering a urinalysis (UA) with or without a culture. However, an ASP has been established in the acute care areas of the facility and an overall hospital antibiogram is available to providers. The institutional review board approved this study as a quality assurance/quality improvement proposal prior to beginning data collection.

Participant Selection

All patients with urine cultures sent from the ED for analysis between October 1, 2015 and November 24, 2015 were included. Patients with long-term indwelling catheters, concurrent antibiotics, and those admitted for inpatient care were excluded from the analysis. For patients with multiple ED visits during the specified time period, only the first drawn urine culture was included in the analysis. Therefore, subsequent urine cultures were considered duplicates and are marked as such in the results.

Study Objectives and Definitions

The primary objective of the study was to determine the frequency of patients discharged from the ED with antibiotic therapy for symptomatic bacteriuria and ASB. The secondary objective was to determine the frequency of appropriate antibiotic prescribing at follow-up, defined as within 48 hours of urine culture results. Safety was assessed by the frequency of antibiotic-related ADRs, including the occurrence of *Clostridium difficile* infections, based on a review of documentation of routine ED follow-up calls and notes for up to 30 days following ED discharge. Definitions of a normal UA, abnormal UA, appropriate antibiotic dose and duration, inappropriate antibiotic treatment, and inappropriately collected urine culture are shown in the appendix.

Figure 1. Study flow chart of patients meeting the inclusion and exclusion criteria.

Data Analysis and Statistics

The list of patients with urine cultures sent from the ED was obtained from the microbiology laboratory. All patient charts were reviewed from the electronic health record and the following data were collected: age, gender, date of ED visit, concurrent medications for benign prostatic hyperplasia or overactive bladder, diagnosis of dementia, UA results, documented UTI symptoms, history of relapsed or recurrent UTI, antimicrobial agent, antibiotic dose and duration, urine culture results, urine culture susceptibilities, ADRs, documented antibiotic allergy, and appropriateness of urine culture collection. SAS version 9.4 (SAS Institute Inc, Cary, NC) was used for data and statistical analyses. *T* tests were applied for normally distributed continuous data. Chi-square test was used for categorical data as appropriate, and Fisher's exact test was used for cells with counts <5. A *P* value of .05 was considered statistically significant.

Results

Number of Participants

Of the 429 ED visits reviewed, 173 patients met the study inclusion and exclusion criteria (Figure 1); the most common reason for exclusion was subsequent admission for inpatient care (69.1%), followed by concurrent antibiotic therapy for a non-UTI indication (13.3%), duplicate cultures (11.3%), and use of chronic bladder management

Table 1. Baseline Demographics.

Variable	Subjects (N = 173)
Male, n (%)	150 (86.7)
Age (in years)	
Mean $\pm$ SD (range)	63.5 $\pm$ 16.4 (25-93)
≥ 85 years, n (%)	15 (8.7)
Antibiotic allergy, n (%)	19 (11.0)
Dementia diagnosis, n (%)	6 (3.5)
Treatment for BPH or OAB, n (%)	50 (28.9)

Abbreviations: BPH, benign prostatic hyperplasia; OAB, overactive bladder.

Table 2. Reasons for Inappropriately Treated Bacteriuria.

Reason	Subjects (N = 13)
Abnormal UA, n (%)	10 (76.9)
Abnormal UA and recent UTI, n (%)	1 (7.7)
Abnormal UA and possible nephrolithiasis, n (%)	2 (15.4)

Abbreviations: UA, urinalysis; UTI, urinary tract infection.

devices (6.3%). Baseline demographics are shown in Table 1. Patients were predominantly male with a mean age of 63.5 $\pm$ 16.4 years. All patients with urine cultures also had UAs completed. The most common bacteria isolated from urine cultures (n = 39) include Gram-positive flora, unspecified (51%); mixed flora, unspecified (12%); *Escherichia coli* (9%); *Klebsiella pneumoniae* (5%); beta-hemolytic *Streptococcus* sp (4%); *Enterococcus faecalis* (4%); *Streptococcus viridans* (3%); and other (12%).

Bacteriuria was treated with an antibiotic in 32.4% (n = 56) of the cohort. Out of the 56 patients treated for a bacteriuria, 76.8% (n = 43) had documented UTI symptoms in the medical record on ED presentation and were treated with antibiotics. The majority of patients received ciprofloxacin (69.6%), followed by cephalexin (17.4%), nitrofurantoin (6.5%), fosfomycin (2.2%), amoxicillin/clavulanate (2.2%), and sulfamethoxazole/trimethoprim (2.2%). Of those cultures with antibiotic sensitivities completed (n = 25 cultures in 25 unique patients), the majority (88.0%) of cultured organisms were susceptible to the prescribed antibiotic. In the absence of any documented sign or symptom potentially attributable to a UTI, 23.2% of 56 patients with ASB received antibiotic therapy and met the definition of inappropriate antibiotic treatment. The most common reason for inappropriate antibiotic treatment for bacteriuria was presence of an abnormal UA (Table 2). Of the 173 patients with a urine culture collected, 40.5% (n = 70) reported urinary symptoms. Of the reported symptoms, urinary frequency and dysuria were most frequent. Symptoms identified in patients with urine cultures are described in Figure 2.

Out of the 56 patients treated for a bacteriuria, 23.2% (n = 13) were identified as requiring postdischarge interventions either due to (1) the cultured organisms being intermediate or resistant to the initial choice of antibiotic (n = 3) or (2) if the patient was initially treated with an antibiotic for a presumed UTI, but had a subsequent negative urine culture (n = 10). Of the 13 patients requiring postdischarge intervention, only 4 patients received appropriate follow-up. These patients had antibiotic therapy switched due to a resistant isolate (2 patients) or the urine cultures collected in the ED were negative (2 patients), and thus the patient was instructed to discontinue the antibiotic prescribed. The remaining 9 patients did not receive appropriate follow-up. One patient grew resistant bacteria without timely antibiotic switch (a change in antibiotic therapy within 2 business days of final culture report), and 8 patients had unaddressed negative urine cultures.

Outcome

A subgroup analysis was performed on 157 patients with either normal (69.4%) or abnormal (30.6%) UAs (16 subjects did not meet the criteria for abnormal or normal UA). As expected, patients with an abnormal UA were older and more likely to have a positive urine culture, report UTI symptoms, and receive an antibiotic ($P < .02$ for all; Table 3). As compared to patients with an abnormal UA, patients with a normal UA were more likely to have a urine culture collected that was not indicated per study definitions ($P = .0008$; see the appendix).

Adverse Events/Safety

There were no significant ADRs identified in the study cohort, including infection with *Clostridium difficile* within 30 days. However, one patient experienced mild loose stools following treatment with ciprofloxacin, which did not necessitate discontinuation of the antibiotic.

Discussion

Inappropriate antibiotic treatment of ASB contributes to increasing rates of antimicrobial resistance. Based on the presence of UTI symptoms, this current study identified higher rates of appropriate antibiotic prescribing (76.8%) compared to prior studies. A recent survey of resident physicians showed only 33.7% were able to distinguish ASB from a true UTI, with half of survey responders reporting prescribing antibiotics for ASB despite awareness of the lack of indication.¹² In a pre- and postintervention study assessing the empiric treatment of patients with UTIs following ED provider education, the adherence rates with IDSA guideline recommendations increased from 44.8% to 83.0%.⁹ Sigler and colleagues conducted a retrospective

Figure 2. Documented symptoms (N = 70)^{a,b}.

^aAMS = altered mental status.

^bThe sum of the columns are >100% because some patients reported multiple symptoms.

Table 3. Subgroup Analysis of Characteristics Associated With Normal and Abnormal UAs.

Variable	Normal UA (n = 109) ^a	Abnormal UA (n = 48) ^a	P
Age in years, mean $\pm$ SD (range)	61.7 $\pm$ 17.1 (25-91)	68.6 $\pm$ 15.0 (26-93)	.0134
UTI symptom present, n (%)	33 (30.3)	29 (60.4)	.0004
Antibiotics received, n (%)	6 (5.5)	42 (87.5)	<.0001
Asymptomatic bacteriuria, treated, n (%)	3 (2.8)	13 (27.1)	<.0001
Culture positive, n (%)	7 (6.4)	27 (56.3)	<.0001
Culture negative, n (%)	102 (93.6)	21 (43.8)	
Inappropriate urine culture collection, ^b n (%)	40 (83.3)	5 (10.4)	.0008

Abbreviations: UA, urinalysis; UTI, urinary tract infection.

^aSixteen patients did not meet criteria for normal or abnormal UA as defined by Table 1.

^bN = 48; 3 patients did not meet criteria for normal or abnormal UA.

chart review of patients diagnosed with UTIs in an outpatient internal medicine clinic and identified 60.7% of patients received appropriate first-line therapy.¹³

ED-specific interventions including development of antibiograms and postprescription culture follow-up in a multidisciplinary approach have been implemented in prior studies.^{10,12,14} Dumkow et al compared the impact of an ED culture follow-up program as compared to a historical standard of care control group. This study found an improved rate of ED revisits and hospital admissions of 10.2% compared to 16.9% in the control group.¹² The authors also identified that 25.0% of patients required postdischarge antibiotic intervention, although they did not report this for controls.¹²

In the past few years, there have been practice changes implemented by the ED at the study institution involving urine culture follow-up. As part of continuous quality improvement efforts we have received feedback on this process from ED providers and identified some challenges. Currently, the microbiology laboratory provides printed

results of all urine cultures obtained in the ED setting to one individual ED provider, who reviews the results and coordinates follow-up if necessary with the patient's primary care provider. As this is not an automatic or an electronic process, some cultures have been overlooked secondary to a paper-dependent activity and work hours of the provider. In light of these issues, incorporating multiple providers, a treatment algorithm, or a dedicated ED clinical pharmacist responsible for this process may minimize these issues. Even with the potential for improvement, we identified a higher frequency of appropriate UTI treatment and follow-up as compared to prior studies. These results may be secondary to the implementation of this current procedure.

Despite these positive findings regarding appropriate prescribing and postdischarge follow-up, there was a fairly high percentage of urine cultures collected when not indicated, with 30.6% of patients having urine cultures collected without any documented symptoms potentially attributable to a UTI. Eighty-three percent of these patients had a subsequent normal urine culture. This suggests that a

large portion of patients are having urine cultures collected and sent for analysis when a UTI is not suspected. This practice adds a cost burden and an increased potential for inappropriate treatment of ASB.^{15,16}

There were also high rates of fluoroquinolone use, with 70% of patients treated receiving ciprofloxacin, similar to past reports in the literature.^{13,17,18} In light of serious adverse effects associated with this antibiotic class, the US Food and Drug Administration released a safety announcement in May 2016 advising against the use of fluoroquinolones for the treatment of uncomplicated UTIs in patients who have alternative treatment options.¹⁹ A local antibiogram of urine cultures may assist with the identification of alternative antibiotics that are likely to be susceptible.²⁰

Limitations

This study was a single-center retrospective chart review of an older patient population over a short time frame. The 30-day follow-up period may have been insufficient to detect serious antibiotic-related adverse events, such as *Clostridium difficile*. The study results were dependent on provider documentation in the electronic health record and subjective assessments of UTI symptoms. There were no direct comparisons made for either the primary or secondary endpoints, and the results of this study can be compared only to frequencies of appropriate antibiotic prescribing in

past studies. Hematuria was also included as a potential UTI symptom. While many studies, including the IDSA guidelines, do not list hematuria as a possible symptom, hematuria was included in the analysis of this study as patients with UTIs often report hematuria.^{1-3,6,9,12} With the inclusion of hematuria in the assessment, there is a possibility of overestimation of the frequency of appropriate antibiotic prescribing. Finally, standard practice in the study ED includes routine follow-up of urine cultures. As compared to prior studies, our results demonstrate high rates of appropriate antibiotic prescribing for UTI treatment and culture follow-up with antibiotic modifications. However, there is also an opportunity for improvement such as automating the process electronically and dedicating personnel, such as an ED clinical pharmacist, to participate in stewardship interventions.

Conclusion

The majority of patients received appropriate initial treatment for bacteriuria based on the presence of associated urinary symptoms. There were few patients requiring post-discharge interventions, 30% of which were addressed appropriately. Incorporating antimicrobial stewardship activities in the ED targeted toward limiting unnecessary urine culture collection and assuring appropriate postdischarge follow-up can improve antibiotic prescribing.

Appendix

Study Definitions.

Term	Definition
Bacteriuria	Two consecutive urine collections with isolates of bacterial strains $\geq 10^5$ CFU/mL in women or $\geq 10^2$ CFU/mL in a single, clean-catch urine specimen in men or catheterized patients ¹
Normal UA	Negative leukocyte esterase and normal WBC count ^a
Abnormal UA	Positive leukocyte esterase and elevated WBC
Appropriate antibiotic selection	Antibiotic prescribed for the treatment of UTI (vs ASB) and appropriate selection of the specific agent in accordance with IDSA guidelines
Appropriate antibiotic prescribing at follow-up (within 48 hours of urine culture results)	If culture is positive, the organism is susceptible to the antibiotic as stated on the culture and sensitivity report. If the organism is not susceptible to the antibiotic selected in the ED, an appropriate antibiotic is prescribed.
Appropriate dose and duration	Dose and duration of antibiotic therapy in accordance with IDSA guidelines
Inappropriate antibiotic treatment	Any antibiotic prescribed for asymptomatic bacteriuria in nonpregnant patients in the absence of other infections
Inappropriately collected urine culture	Urine culture collected from a patient with no documented signs or symptoms potentially attributable to a UTI

Abbreviations: CFU, colony forming unit; UA, urinalysis; WBC, white blood cell; UTI, urinary tract infection; ASB, asymptomatic bacteriuria; IDSA, Infectious Diseases Society of America; ED, emergency department.

^aOnly negative leukocyte esterase if WBC count not reported.

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References

1. Nicolle LE, Bradley S, Colgan R, Rice JC, Schaeffer A, Hooton TM. Infectious Diseases Society of America guidelines for the diagnosis and treatment of asymptomatic bacteriuria in adults. *Clin Infect Dis*. 2005;40:643-654. doi:10.1086/427507.
2. Coyle EA, Prince RA. Urinary tract infections and prostatitis. In: DiPiro JT, Talbert RL, Yee GC, et al, eds. *Pharmacotherapy: A Pathophysiologic Approach*. 9th ed. New York, NY: McGraw-Hill; 2014:1849-1867.
3. Schaeffer AJ, Nicolle LE. Urinary tract infections in older men. *N Engl J Med*. 2016;374:562-571. doi:10.1056/NEJMc1503950.
4. Grover ML, Bracamonte JD, Kanodiq AK, et al. Assessing adherence to evidence-based guidelines for the diagnosis and management of uncomplicated urinary tract infection. *Mayo Clin Proc*. 2007;82:181-185. doi:10.4065/82.2.181.
5. Willems L, Denckens P, Philips H, Henriquez R, Remmen R. Can we improve adherence to guidelines for the treatment of lower urinary tract infection? A simple, multifaceted intervention in out-of-hours services. *J Antimicrob Chemother*. 2012;67:2997-3000. doi:10.1093/jac/dks336.
6. Rotjanapan P, Dosa D, Thomas KS. Potentially inappropriate treatment of urinary tract infections in two Rhode Island nursing homes. *Arch Intern Med*. 2011;171:438-443. doi:10.1001/archinternmed.2011.13.
7. Infectious Diseases Society of America. Combating antimicrobial resistance: policy recommendations to save lives. *Clin Infect Dis*. 2011;52(suppl 5):S397-S428. doi:10.1093/cid/cir153.
8. Pulcini C. Antimicrobial stewardship in emergency departments: a neglected topic. *Emerg Med J*. 2015;32:506. doi:10.1136/emermed-2014-204220.
9. Percival KM, Valenti KM, Schmittling SE, Strader BD, Lopez RR, Bergman SJ. Impact of an antimicrobial stewardship intervention on urinary tract infection treatment in the ED. *Am J Emerg Med*. 2015;33:1129-1133. doi:10.1016/j.ajem.2015.04.067.
10. Trinh TD, Klinker KP. Antimicrobial stewardship in the emergency department. *Infect Dis Ther*. 2015;4(suppl 1):S39-S50. doi:10.1007/s40121-015-0084-8.
11. Zhang X, Rowan N, Pflugeisen BM, Alajbegovic S. Urine culture guided antibiotic interventions: a pharmacist driven antimicrobial stewardship effort in the ED. *Am J Emerg Med*. 2017;35:594-598. doi:10.1016/j.ajem.2016.12.036.
12. Dumkow LE, Kenney RM, MacDonald NC, Carreno JJ, Malhotra MK, Davis SL. Impact of a multidisciplinary culture follow-up program of antimicrobial therapy in the emergency department. *Infect Dis Ther*. 2014;3:45-53. doi:10.1007/s40121-014-0026-x.
13. Sigler M, Leal JE, Bliven K, Cogdill B, Thompson A. Assessment of appropriate antibiotic prescribing for urinary tract infections in an internal medicine clinic. *South Med J*. 2015;108:300-304. doi:10.14423/SMJ.0000000000000278.
14. Baker SN, Acquisto NM, Ashley ED, Fairbanks RJ, Beamish SE, Haas CE. Pharmacist-managed antimicrobial stewardship program for patients discharged from the emergency department. *J Pharm Pract*. 2012;25:190-194. doi:10.1177/0897190011420160.
15. Cope M, Cevallos ME, Cadle RM, Darouiche RO, Musher DM, Trautner BW. Inappropriate treatment of catheter-associated asymptomatic bacteriuria in a tertiary care hospital. *Clin Infect Dis*. 2009;48:1182-1188. doi:10.1086/597403.
16. Yin P, Kiss A, Leis JA. Urinalysis orders among patients admitted to the general medicine service. *JAMA Intern Med*. 2015;175:1711-1713. doi:10.1001/jamainternmed.2015.4036.
17. Bishop BM. Antimicrobial stewardship in the emergency department: challenges, opportunities, and a call to action for pharmacists. *J Pharm Pract*. 2016;29:556-563. doi:10.1177/0897190015585762.
18. Werner NL, Hecker MT, Sethi AK, Donskey CJ. Unnecessary use of fluoroquinolone antibiotics in hospitalized patients. *BMC Infect Dis*. 2011;11:187. doi:10.1186/1471-2334-11-187.
19. Food and Drug Administration. Fluoroquinolone antibacterial drugs: drug safety communication—FDA advises restricting use for certain uncomplicated infections. <http://www.fda.gov/Safety/MedWatch/SafetyInformation/SafetyAlertsforHumanMedicalProducts/ucm500665.htm>. Published July 26, 2016. Accessed March 14, 2017.
20. Draper HM, Farland JB, Heidel RE, May LS, Suda KJ. Comparison of bacteria isolated from emergency department patients versus hospitalized patients. *Am J Health Syst Pharm*. 2013;70:2124-2128. doi:10.2146/ajhp130079.