Infection Control & Hospital Epidemiology (2020), **41**, 1090–1092
doi:10.1017/ice.2020.230

Concise Communication

Unintended consequences of a reflex urine culture order set on appropriate antibiotic use

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Abstract

We evaluated the impact of reflex urine culture screen results on antibiotic initiation. More patients with positive urine screen but negative culture received antibiotics than those with a negative screen (30.5 vs 7.1%). Urine screen results may inappropriately influence antibiotic initiation in patients with a low likelihood of infection.

(Received 5 November 2019; accepted 4 May 2020; electronically published 23 June 2020)

As much as 43% of inpatient cases of asymptomatic bacteriuria are treated with antibiotics,[1] and efforts to reduce unnecessary antibiotic use have increasingly focused on diagnostic stewardship.[2,3] Moving to reflex testing has been one method used by institutions to reduce urine culture in asymptomatic patients and thus reduce excess use of antimicrobials. However, the degree to which the urine screen result itself influences antibiotic initiation remains unknown.[4] We compared antibiotic ordering in hospitalized patients with negative urine screens to those with positive urine screens and negative cultures.

Methods

Study setting

The Oregon Health & Science University (OHSU) is 556-bed, quaternary-care, academic healthcare facility located in Portland, Oregon. Criteria for reflex urine cultures were any of the following: presence of nitrites, leukocyte esterase, bacteria, or white blood cell count $\geq 5 \times 10^9$ cells/L. If any of the criteria were met, an intermediate result was reported as "POSITIVE" in a bold red font in the microbiology results section of the medical record, prior to culture result availability.

We conducted a retrospective, cross-sectional study among patients admitted to OHSU between January 1 and June 30, 2015. Adult patients (≥18 years old) with a length of stay >24 hours and urine test that resulted in either a negative screen or a positive screen with a subsequent negative culture were eligible for inclusion. Among these, only the first urine screen performed during the admission was included for analysis. Patients with a history of transplant in the year prior, urologic surgery in the 30 days prior to hospitalization, current pregnancy, or antibiotics administrated before urine reflex results were available were excluded.

Data collection

Patient characteristics and urine test information were electronically abstracted from the pharmacy research repository that stores clinical, laboratory, and administrative data from OHSU's electronic health record and is maintained through support from the Oregon Clinical Translational and Research Institute.

We conducted a chart review using an electronic data collection template to confirm study eligibility and to collect additional data: comorbidities that might impede urinary flow; urinary catheter characteristics (placement date and time, duration); admission characteristics (chief complaint, transfer status); and urinary symptoms prior to urine sample collection (suprapubic pain, dysuria, frequency, or urgency). For the first antibiotic ordered, we recorded whether a urinary tract infection (UTI) was documented as the indication for the order; in cases where multiple antibiotics were ordered, the broader-spectrum anti-UTI agent was selected for analysis. The investigator performing chart review was blinded to the reflex results.

The primary exposure, urine screen result, was classified as reflex positive with a subsequent negative culture versus a reflex negative urine screen. Individual components of the urine screen results (ie, presence of nitrites, leukocyte esterase, white blood cells, and bacteria) were also collected. The primary outcome of interest was prescription of an anti-UTI antibiotic within 48 hours of the urine screen result.

Data analysis

Patient and clinical characteristics were compared between patients with a positive urine culture reflex screen, culture-negative

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PREVIOUS PRESENTATION. Preliminary data from this research were previously presented at IDWeek 2015 on October 10, 2015, in San Diego, California.

Cite this article: Klein CN, *et al.* (2020). Unintended consequences of a reflex urine culture order set on appropriate antibiotic use. *Infection Control & Hospital Epidemiology*, 41: 1090–1092, https://doi.org/10.1017/ice.2020.230

Table 1. Patient Characteristics and Antibiotic Prescribing by Urine Screen Result

Characteristic	Urine Screen Positive (n=703), No. (%)[a]		Urine Screen Negative (n=1,241), No. (%)[a]	
Sex, female	457	(65.0)	438	(35.3)
Race, white	601	(85.5)	1,032	(83.2)
Non-Hispanic	641	(91.2)	1,144	(92.2)
Age at admission, mean (SD)	56.6	(19.2)	54.9	(18.8)
Admitted from emergency department	476	(67.7)	916	(73.8)
Comorbidities				
Diabetes	187	(26.6)	294	(23.7)
Uropathy or other urinary tract abnormalities	41	(5.8)	37	(3.0)
Abnormal outflow	11	(1.6)	3	(0.2)
Urinary catheter[b]				
Present	131	(18.6)	136	(11.0)
Duration, median (IQR)	67.0	(36.0–119.0)	46.5	(26.5-93.0)
Neutropenic	1	(0.1)	12	(1.0)
Urinary symptoms				
Symptoms documented	52	(7.4)	49	(3.9)
Documentation states no symptoms	513	(73.0)	965	(77.8)
Unclear documentation	138	(19.6)	227	(18.3)
Antibiotic ordered[c]	99	(14.1)	31	(2.5)
Antibiotic				
Ceftriaxone	42	(42.4)	8	(25.8)
Ciprofloxacin	24	(24.2)	7	(22.6)
Trimethoprim/Sulfamethoxazole	8	(8.1)	5	(16.1)
Nitrofurantoin	8	(8.1)	2	(6.5)
Piperacillin/Tazobactam	5	(5.1)	4	(12.9)
Other	12	(12.1)	5	(16.1)
Hours between reflex result and antibiotic order, median (IQR)	3.0	(1.0–11.0)	7.0	(2.0–30.0)

Note. SD, standard deviation; IQR, interquartile range.
[a]Unless otherwise indicated.
[b]Urinary catheter in place during urine test order.
[c]χ^2 test, $P < .001$.
[d]Fisher exact test, $P = .179$.
[e]Wilcoxon-Mann-Whitney test, $P = .024$.

patients, and screen-negative patients using the χ^2 or the Fisher exact test for categorical variables and the Wilcoxon-Mann-Whitney test for continuous variables. Multivariable logistic regression was performed to assess the independent association between reflex status and prescription of an anti-UTI agent. The following covariates were evaluated for inclusion: sex, age, white race, non-Hispanic ethnicity, admission through emergency department, diabetes, urinary symptoms, and presence of an indwelling catheter at the time of urine specimen collection. Backward-stepwise selection with $P < .20$ entry and $P < .05$ exit criteria were used to identify significant covariates. Confounders, defined as covariates whose inclusion affects a 10% or greater change in the estimated odds ratios between reflex result status and UTI antibiotic prescription were also retained. We also tested whether the presence of a Foley catheter was an effect modifier for the association between reflex status and receipt of an anti-UTI antibiotic, which had been determined a priori. All P values were 2-sided and the significance level was set at 0.05. Adjusted odds ratios (aOR) and 95% confidence intervals (CI) from the final model are reported. All analyses were performed with SAS version 9.2 software (SAS Insitute, Cary, NC). This study was approved by the OHSU Institutional Review Board.

Results

In total, 10,178 adult patients were identified as having been admitted for >24 hours at OHSU during the 6-month study period. Of the 1,944 patients who met our inclusion criteria, 1,241 (63.8%) had a negative reflex result and 703 (36.2%) had a positive reflex result with subsequent negative urine culture. Demographic characteristics were similar among patients with and without a positive reflex (Table 1), except that a greater proportion of females had positive reflex results compared with males (65.0 vs 35.3%). Patients with a positive reflex had higher proportions of comorbidities than those with negative results: diabetes (26.6 vs 23.7%), uropathy or other urinary tract abnormalities (5.8 vs 3.0%), and abnormal outflow (1.6 vs 0.2%). Compared to those with a

https://doi.org/10.1017/ice.2020.230 Published online by Cambridge University Press

negative reflex, inpatients with a positive reflex had a higher proportion of indwelling urinary catheter (18.6 vs 11.0%) as well as a longer duration of catheterization (67.0 vs 46.5 hours). Patients with positive reflex results also had a greater proportion of urinary symptoms documented in their chart than those with negative findings (7.4 vs 3.9%).

In total, 130 patients (6.7%) received a urinary antibiotic after urine screening results were reported. A greater proportion of patients with a positive screen received anti-UTI antibiotics than those with a negative screen (14.1 vs 2.5%; χ^2 test, $P < .01$). The most commonly prescribed agents were ceftriaxone (38.5%), ciprofloxacin (23.8%), and trimethoprim/sulfamethoxazole (10.0%). Choice of antibiotic did not significantly differ by urine screen status (Table 1). Reflex positive patients had antibiotics ordered more quickly (median, 3.0 hours) than the reflex negative group (median, 7.0 hours; $P = .02$).

Further analysis revealed that 606 patients (31.2%) had both urinary antibiotic prescriptions and nonambiguous documentation of urinary symptoms. Reflex positive testing was significantly associated with urinary antibiotic prescription (aOR, 4.92; 95% CI, 3.04–7.96) after adjusting for the presence of urinary symptoms. The presence of urinary symptoms was an independent predictor of urinary antibiotic prescription (aOR, 8.99; 95% CI, 4.86–16.63).

Discussion

To limit unnecessary urine culturing and simplify the ordering process, many institutions have enacted a single UTI panel order set that sends samples first for urinalysis and then automatically reflexes samples for culture if the initial screen is positive. Screening criteria are often created to be highly sensitive to ensure that true infections are cultured. We observed that patients with a positive urine screen but negative culture were significantly more likely to have an antibiotic initiated than those with a negative urine screen. This finding suggests that the results of the urine screen itself influences the decision to initiate therapy. This conclusion is supported by the observation that antibiotics were initiated more often and more quickly for patients with a positive screen result. The retrospective nature of this study limited our ability to conclusively attribute urine screen test results to the decision to prescribe antibiotics. Nevertheless, antibiotic stewardship programs rely on retrospective assessments to identify targets for intervention. Our findings suggest that urine reflex screens may inappropriately influence the decision to initiate antibiotic therapy at our institution and can serve as a target of intervention.

Acknowledgments. None.

Financial support. These research activities were performed with the support of Oregon Clinical and Translational Research Institute (CTSA award no. UL1TR002369).

Conflicts of interest. Dr. McGregor reports grants from Merck & Co outside the submitted work. All other authors have nothing to disclose.

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https://doi.org/10.1017/ice.2020.230 Published online by Cambridge University Press