Poster # 5618

Impact of Urine Analysis Methods in the Diagnosis of Uncomplicated Urinary Tract Infection

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ABSTRACT

BACKGROUND: Acute urinary tract infection (UTI) results in 13.5 million office or emergency room visits and 21 million prescriptions in the United States annually. Non-culture methods, including detection of pyuria and bacteriuria by dipstick and/or microscopy, are commonly used to inform clinicians whether to prescribe empiric antibiotics. Urine dipstick is readily available in the outpatient setting, but the performance characteristics of the leukocyte esterase (LE) and nitrite (N) tests, alone or in combination, vary; in general, the two tests used together perform better than either test used alone, and the tests are better at detecting bacteriuria at high colony counts than at low colony counts. Other factors may impact the performance characteristics of the LE and N tests, including whether the strip is read by visual inspection or by machine.

METHODS: As part of an open label study of oral ciprofloxacin for adult women with uUTI at 20 U.S. sites, we analyzed the performance characteristic for LE and N, focusing on whether strips were read by visual inspection or by machine. All patients enrolled had at least two of five classic uUTI symptoms and a positive urine dipstick for both LE and N. Post-enrollment, prior to treatment, patient's urine was collected and sent to the local laboratory for culture and sensitivity. Initially, sites followed their usual standard of care and read the dipsticks either visually or with an automated reader. Part-way through the study, sites were provided an automated dipstick analyzer machine (McKesson Consult® 120 Urine Analyzer) which was employed for the remainder of the study.

RESULTS:

Method*	N	Number (%) Cultures Positive**	p value
Machine read	53	42 (79.2)	0.046
Visual inspection	128	82 (64.1)	

*Dipstick Positive for both LE and N; ** for ≥10^5 CFU/mL of a Uropathogen

CONCLUSIONS: Visual inspection of urine dipsticks is a subjective process that may lead to misinterpretation of results. Using an automated urine dipstick reader to identify specimens positive for both LE and N showed an improved culture positivity rate over those identified as double-positive by visual inspection. There is a need for more accurate methods to identify patients with uUTI.

INTRODUCTION

Acute urinary tract infection (UTI) results in 13.5 million office or emergency room visits and 21 million prescriptions in the United States annually. The presence of classic UTI symptoms and non-culture examination of the urine, including detection of pyuria and bacteriuria by dipstick and/or microscopy, are commonly used to inform clinicians whether to prescribe empiric antibiotics. Urine dipstick is the most common non-culture test utilized by clinicians. It is readily available in the outpatient setting, but the performance characteristics of the leukocyte esterase (LE) and nitrite (N) tests, alone or in combination, vary; in general, the two tests used together perform better than either test used alone, and the tests are better at detecting bacteriuria at high colony counts than at low colony counts. While the urine dipstick test is a seemingly straightforward point-of-care (POC) test to perform, there may be unrealized factors that impact the performance characteristics of the LE and N tests, including whether the strip is read by visual inspection or by machine.

METHODS

As part of an open label study of oral ciprofloxacin for adult women with uUTI at 20 U.S. sites, we analyzed the performance characteristic for LE and N, focusing on whether strips were read by visual inspection or by machine. All patients enrolled had at least two of five classic uUTI symptoms and a positive urine dipstick for both LE and N. Post-enrollment, prior to treatment, patient's urine was collected and sent to the local laboratory for culture and sensitivity. Initially, sites followed their usual standard of care and read the dipsticks either visually or with an automated reader. Part-way through the study, sites were provided an automated dipstick analyzer machine (McKesson Consult® 120 Urine Analyzer) which was employed for the remainder of the study

RESULTS

Table 1. Baseline Demographics

Characteristic	Total (N=250)
Age, years	
Mean (SD)	47.3 (16.0)
Median	46.0
Sex, n (%)	
Female	250 (100.0)
Race, n (%)	
White	202 (80.8)
Black or African American	42 (16.8)
Asian	4 (1.6)
Other	2 (0.8)
Ethnicity, n (%)	
Hispanic/Latino	147 (58.8)
Not Hispanic/Latino	98 (39.2)
Not Reported/Unk	5 (2.0)
BMI, kg/m²	
Mean (SD)	29.01 (6.9)
BMI Distribution	
BMI > 30 kg/m²	91 (36.5)
Diabetes, n (%)	25 (10.0)

RESULTS

Table 2. Summary of Baseline Signs & Symptoms of uUTI (ITT)

Characteristic	Total
Gross hematuria	
Absent	141/180 (78.3)
Mild	22/180 (12.2)
Moderate	11/180 (6.1)
Severe	6/180 (3.3)
Pain/burning with urination	
Absent	23/180 (12.8)
Mild	38/180 (21.1)
Moderate	62/180 (34.4)
Severe	57/180 (31.7)
Lower abdominal pain	
Absent	21/180 (11.7)
Mild	26/180 (14.4)
Moderate	93/180 (51.7)
Severe	40/180 (22.2)
Urinary frequency	
Absent	3/119 (2.5)
Mild	13/119 (10.9)
Moderate	34/119 (28.6)
Severe	69/119 (58.0)
Urinary urgency	
Absent	8/119 (6.7)
Mild	12/119 (10.1)
Moderate	38/119 (10.1)
Severe	61/119 (51.3)
Frequency and urgency	
Absent	1/61 (1.6)
Mild	16/61 (26.2)
Moderate	21/61 (34.4)
Severe	23/61 (37.7)

Table 3. Baseline Uropathogens (Micro-MITT)

Baseline Pathogens	Total (N=124) n(%)
Number of Subjects with at least one Pathogen at Baseline	124 (100.0)
Escherichia coli	108 (87.1)
Klebsiella species	13 (10.5)
Proteus mirabilis	3 (2.4)
Enterobacter cloacae	2 (1.6)
Morganella morganii	1 (0.8)
Staphylococcus saprophyticus	1 (0.8)

Table 4. Urine Dipstick: Machine Read *vs* Visual Inspection

Method*	N	Number (%) Cultures Positive**	p value
Machine read	53	42 (79.2)	0.046
Visual inspection	128	82 (64.1)	

*Dipstick Positive for both LE and N; ** for ≥10^5 CFU/mL of a Uropathogen

Table 5. Lab-based UA Results: Patients with +/+ Dipstick by POC Testing

Leukocyte Esterase	Nitrite	N*	Number (%) Cultures Positive**
+	+	80	66 (82.5)
+	-	63	38 (60.3)
-	+	8	7 (87.5)
-	-	9	3 (33.3)

*missing UA data for 21 patients; **for ≥10^5 CFU/mL of a uropathogen

Table 6. +/+ Lab-based UA Result After Having a +/+ POC Test

Method	N	Number (%) Cultures Positive**
+/+ by Machine at POC	30	26 (86.7)
+/+ by Visual Inspection at POC	50	40 (80.0)

Table 7. Features of Urine Dipstick Tests in Diagnosis of UTI

Urine Dipstick Test	Features	False Positives	False Negatives
Leukocyte esterase	WBCs in urine release this granulocytic esterase → cleaves indoxyl or pyrole ester → free indoxyl or pyrole reacts with diazonium salt → purple color, intensity of color is proportional to number of WBCs present in specimen, detects intact and lysed cells, need to wait 2 minutes before reading test strip manually, sensitivity 5-15 WBC/hpf	Contamination of urine with vaginal secretions, WBCs present in urine from inflammatory process such as vaginitis or sexually transmitted infection, expired, contaminated, or improperly stored test strips, increased cell lysis in setting of low specific gravity, waiting too long to read test strip manually	Specimen not mixed well or at low temperature, low bacteria colony count in early UTI, bacterial inhibition by antibiotics, glycosuria, proteinuria, decreased cell lysis in setting of high specific gravity, presence of oxidizing drugs (cephalexin, nitrofurantoin, tetracycline, gentamicin, vitamin C), high concentration of oxalic acid, boric acid, sodium azide, mercury salts, or hydrochloric acid, failure to wait 2 minutes to read test strip manually
Nitrite	Absent from normal urine, most Enterobacteriaceae reduce urinary nitrates to nitrites using nitrate reductase enzyme → nitrite interacts with aromatic amine and diazonium compound → pink color, intensity of color is measure of nitrite concentration, pink spots or pink edges should not be interpreted as a positive result, at least 4 hours required for bacteria in bladder to convert nitrate to nitrite at reliably detectable levels, need to wait 1 minute before reading test strip manually, sensitivity 0.06-0.1 mg/dL nitrite ion	Contamination of urine with perineal or periurethral bacteria, improper storage of urine prior to testing, expired, contaminated, or improperly stored test strips, red-colored food or drugs including phenazopyridine, waiting too long to read test strip manually	Infection due to a nitrate reductase-negative bacteria (*S. saprophyticus*, Enterococcus, Pseudomonas), insufficient duration of urine retention in bladder before giving specimen, low bacteria colony count in early UTI, presence of oxidizing drugs (cephalexin, nitrofurantoin, tetracycline, gentamicin, vitamin C), bacterial inhibition by antibiotics, high specific gravity, highly buffered alkaline urine, glycosuria, proteinuria, deficient/absent dietary nitrate, failure to wait 1 minute to read test strip manually

CONCLUSIONS

- ✓ Urine dipstick is the most commonly used non-culture test by clinicians to inform whether to prescribe empiric antibiotics
- ✓ Numerous factors may result in false-positive or false-negative urine dipstick results
- ✓ Visual inspection of urine dipsticks is a subjective process, and misinterpretation of results may occur
- ✓ Automated urine dipstick readers, both POC and lab-based, may improve the accuracy of identifying specimens positive for both LE and N
- ✓ Automated dipstick readers, both POC and lab-based, may improve the culture positivity rate versus visual inspection
- ✓ There is a need for more accurate methods to identify patients with uUTI

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