CONCISE COMMUNICATION

Evaluation of a Healthcare-Associated Urinary Tract Infection Combination Antibiogram

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We created a 2013 combination antibiogram of healthcare-associated urinary tract infection. The 2013 antibiogram–determined regimen was evaluated in a 2014 cohort who had received empirical therapy. The regimen was statistically more likely to represent adequate treatment than actual prescriptions. A customized antibiogram may guide empirical therapy for specific patients.

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The 2014 updated Clinical and Laboratory Standards Institute guidelines emphasize the value of an "enhanced antibiogram," which is stratified by infection characteristics and includes features such as susceptibilities for antibiotic combinations.[1]

The objective of this study was to apply the weighted-incidence syndromic combination antibiogram to healthcare-associated (HA) infections. The weighted-incidence syndromic combination antibiogram, developed by Hebert et al[2] in 2012, is a method of combining all bacterial species and showing percentages susceptible to antibiotic combinations. We specifically chose urinary tract infection (UTI) owing to its high prevalence and well-established criteria for true infection versus colonization. We focused on HA-UTI because choice of empirical therapy, which occurs before the pathogen and its susceptibility are determined, is complicated by the increasing resistance and heterogeneity of organisms causing HA infections. This results in frequent inadequate empirical antibiotic therapy for HA-UTI, with rates as high as 30.5% to 67%.[3,4]

METHODS

The study was conducted at Tufts Medical Center, a 415-bed, level I trauma and tertiary care center in Boston, Massachusetts. The novel antibiogram included urine cultures from 2013 adult inpatients. HA-UTI isolates were defined as positive cultures collected on the third hospital day and later. Cultures growing greater than 1×10^3 colony-forming units/mL were included. Intermediate resistance was considered resistance. The first isolate of the same species was included for each patient, and up to 2 organisms in a single urine culture could be attributed to a patient. In cultures with 2 organisms, susceptibility for each organism was considered without relation to the other. Because susceptibility to every antibiotic used in the antibiogram was not reported for each organism (eg, vancomycin susceptibility of gram-negative organisms), assumptions of antibiotic susceptibility were used on the basis of a published list[2] as well as the expert opinion of our antimicrobial stewardship team. An organism was considered susceptible to the dual regimen if it was susceptible to at least 1 of the 2 antibiotics. Dual regimens required additional assumptions for isolates in which only 1 of the antibiotics had been tested, and these were again determined by expert opinion.

An additional antibiogram was created for symptomatic HA-UTI and compared with the original HA-UTI combination antibiogram for notable differences. Symptomatic UTI was defined as urinalysis consistent with UTI and at least 1 documented UTI symptom in the medical record (fever, urgency, frequency, dysuria, suprapubic tenderness, or costovertebral angle pain).

We validated the 2013 HA-UTI combination antibiogram on 2014 HA-UTI isolates by assessing adequacy of empirical therapy. An empirical antibiotic was administered within 24 hours before or after the urine specimen collection. Electronic discharge summaries were reviewed to determine whether an antibiotic was prescribed for reasons other than presumed UTI, and these isolates were excluded. The percentage of isolates that would have been covered by the 2013 antibiogram-determined optimal regimen was calculated.

Statistical analysis was performed using SPSS, version 22.0 (IBM). The association between the percentage susceptible for the regimen from the 2013 novel antibiogram and that of the empirically prescribed regimens in 2014 was tested with a McNemar test. $P < .05$ was considered statistically significant.

RESULTS

The 2013 HA-UTI combination antibiogram (Table 1) included 235 bacterial isolates (200 unique patients). Single antibiotics were associated with a low percentage of susceptible organisms; only piperacillin-tazobactam exceeded 80% likelihood of susceptibility, the threshold commonly considered for minimum adequacy of an empirical regimen.[5] As expected, isolates were more likely to be susceptible to antibiotic combinations, and 6 of the 10 combinations had susceptibility higher than 80%. The regimen with the highest percentage of susceptible isolates was vancomycin with meropenem (95%).

Of the 235 total isolates included in the 2013 HA-UTI combination antibiogram, 74 were from patients with a positive urinalysis *and* documented symptom (68 unique patients). The organism distribution and susceptibilities of the 2013 symptomatic HA-UTI combination antibiogram were comparable with those of the entire 2013 HA-UTI combination antibiogram, with vancomycin plus meropenem susceptibility at 94% compared with 95%.

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TABLE 1. HA-UTI Combination Antibiogram January-December 2013

Percent susceptible																
IN-PATIENT, Urine adult	Penicillins & related antibiotics					Cephalosporins 1st 3rd generation 4th					Aminoglycosides			Quinolone	Other		UTI agent
	AMPICILLIN (187)	AMPICILLIN / SULBACTAM (202)	PIPERACILLIN /TAZOBACTAM (219)	MEROPENEM (223)	ERTAPENEM (231)	CEFAZOLIN (229)	CEFOXITIN (194)	CEFTAZIDIME (209)	CEFTRIAXONE (224)	CEFEPIME (232)	GENTAMICIN (232)	TOBRAMYCIN (230)	AMIKACIN (235)	CIPROFLOXACIN (229)	TRIMETHOPRIM/SULFA (219)	VANCOMYCIN (217)	NITROFURANTOIN (221)
	50	60	83	75	68	37	53	67	62	75	67	66	71	64	58	18	57

Percent susceptible										
IN-PATIENT, Urine adult	Antibiotic combinations									
	VANCOMYCIN + PIPERACILLIN/TAZOBACTAM (222)	VANCOMYCIN + MEROPENEM (207)	VANCOMYCIN + ERTAPENEM (214)	VANCOMYCIN + CEFTRIAXONE (209)	VANCOMYCIN + CEFEPIME (214)	TOBRAMYCIN + PIPERACILLIN/TAZOBACTAM (230)	TOBRAMYCIN + MEROPENEM (229)	TOBRAMYCIN + ERTAPENEM (233)	TOBRAMYCIN + CEFEPIME (233)	CIPROFLOXACIN + TRIMETHOPRIM/SULFA (225)
	87	95	87	81	93	90	76	75	76	71

NOTE. N = 235 adult inpatient healthcare-associated urinary tract infection (HA-UTI) urine isolates. Data are expressed as n (%) susceptible.

Within the 2014 HA-UTI bacterial isolates, there were 108 isolates (93 unique patients) from patients who were given an empirical antibiotic (Table 2). The organism distribution was very similar to those of the 2013 HA-UTI combination antibiograms. Of the 108 isolates, 31 (28.7%) were treated with inadequate empirical antibiotics. *Enterococcus faecalis* was the species most likely to be treated with an inadequate antibiotic, accounting for 35.5% of all inadequate prescriptions. Of the antibiotics for HA-UTI prescribed in 2014, ciprofloxacin was the most frequent empirical regimen, comprising nearly a third of all prescriptions, and was adequate for 77.1% of cases in which it was prescribed (Table 2). In total, the empirical antibiotics were adequate for 71.3% of the isolates, and vancomycin with meropenem, which was not prescribed for any of the patients, would have been adequate for 92.6% of isolates (Table 2). The combination of vancomycin with meropenem was associated with a statistically significantly higher percentage of susceptible isolates than that of the actually prescribed empirical regimens ($P < .001$).

DISCUSSION

In this study, we showed that an antibiogram specific for HA-UTI including dual regimens identifies distinct susceptibility patterns, which could guide empirical treatment to ensure a higher likelihood of adequate therapy. We also found that pathogen susceptibility was similar between general

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TABLE 2. Regimens of 2014 HA-UTI Empirical Antibiotic Therapy

Antibiotic regimen	Prescribed, no. (%)	Adequate, no. (% of prescribed)
Ciprofloxacin	35 (32.4)	27 (77.1)
Ceftriaxone	19 (17.6)	12 (63.2)
Vancomycin & cefepime	15 (13.9)	14 (93.3)
Trimethoprim/sulfa	9 (8.3)	6 (66.7)
Nitrofurantoin	7 (6.5)	4 (57.1)
Cefazolin	4 (3.7)	2 (50.0)
Vancomycin	3 (2.8)	1 (33.3)
Linezolid	3 (2.8)	3 (100.0)
Cefepime	2 (1.9)	2 (100.0)
Meropenem	2 (1.9)	2 (100.0)
Ertapenem	2 (1.9)	1 (50.0)
Vancomycin & piperacillin/tazobactam	2 (1.9)	1 (50.0)
Ciprofloxacin & trimethoprim/sulfa	2 (1.9)	1 (50.0)
Ciprofloxacin & cefazolin	1 (0.9)	0 (0)
Amikacin and meropenem	1 (0.9)	0 (0)
Aztreonam	1 (0.9)	1 (100)
Total	108 (100)	77 (71.3)

NOTE. N = 108 adult inpatient healthcare-associated urinary tract infection (HA-UTI) urine isolates treated with empirical antibiotic therapy.

antibiograms and symptomatic infections; therefore the need for isolating symptomatic isolates is unnecessary.

Despite the overall low susceptibility in the traditional antibiogram, and the well-documented rise of fluoroquinolone resistance in urinary pathogens,[6,7] ciprofloxacin was the most commonly prescribed regimen in 2014, prescribed for 32.4 % of isolates. In total, empirical antibiotics were inadequate in nearly a third of the cases. This finding indicates a need to continue to educate prescribers about antimicrobial resistance in HA infections and the difference between community-acquired and hospital-acquired pathogens.[5]

Retrospective studies have inherent limitations, and determining true UTI from medical records was imperfect. Patients with only 1 symptom of UTI may in fact have been colonized rather than infected, and this could be particularly true for patients who had cultures positive for *Enterococcus*.

The charge of the antimicrobial stewardship team is to ensure that the optimal drug, dose, and duration of antimicrobial therapy are used, based on the likelihood of various organisms being the cause of infection, and while minimizing "collateral damage." Although we showed that vancomycin with meropenem is the regimen with the highest percentage of susceptible HA-UTI isolates at our institution, there are concerns besides susceptibility to consider when selecting an antibiotic regimen, including development of resistance, depletion of normal microbial flora resulting in *Clostridium difficile* infection, adverse effects, and financial costs of the drug. Urinary tract infection, compared with other HA infections, is associated with relatively low morbidity and mortality. One could argue that achieving the highest possible rate of successful microbial coverage is not necessarily the ultimate goal with this infection.

Therefore, this type of antibiogram could be used in several approaches: (1) Select a narrow-spectrum agent above a certain threshold as the empirical recommendation for lower-risk patients. (2) Recommend the regimen with the highest percentage of susceptible isolates for patients with a higher risk of sepsis. (3) Apply this method to infections associated with increased severity, such as pneumonia or intra-abdominal infection.

Our study has demonstrated the feasibility of producing a customized antibiogram and suggests it is a better reflection of bacterial susceptibility.

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