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BRIEF COMMUNICATION

Antimicrobial susceptibility patterns among *Escherichia coli* urinary isolates from community-onset health care-associated urinary tract infection

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Urinary tract infection (UTI) is traditionally classified as community-acquired (CA) and hospital-acquired (HA). Community-onset health care-associated (HCA) infection is a new category that has gained increasing attention. The study aimed to compare the disk susceptibility of nonrepetitive *Escherichia coli* urinary isolates from HCA-UTI ($n = 100$) with that of *E. coli* isolates from CA-UTI ($n = 85$) and HA-UTI ($n = 106$). We found that the susceptibility pattern of HCA-UTI *E. coli* isolates was similar to that of HA-UTI *E. coli* isolates, but significantly different from that of CA-UTI *E. coli* isolates. In particular, the proportion of extended-spectrum β-lactamase-producing isolates was significantly higher in HCA-UTI than that in CA-UTI (30.0% vs. 3.5%, $p < 0.001$). We recommend that when treating HCA-UTI, it is necessary to take urine cultures for susceptibility testing to guide definite antibiotic therapy.

Introduction

Urinary tract infection (UTI) is one of the most frequent infectious diseases among hospital-acquired (HA) or community-acquired (CA) infections. In order to achieve a satisfactory therapeutic effect, it is suggested that local information regarding the antimicrobial resistance of frequent pathogens should be established as a reference for the selection of empirical antimicrobial therapy.[1,2]

Microorganisms for CA-UTI are usually associated with a lower level of antimicrobial resistance, whereas higher resistance rates or, even worse, multidrug resistance are rather common among HA-UTI pathogens.[3] In the past few decades, improvement in the medical management has made some traditionally inpatient procedures to be delivered on an outpatient basis. Infections developed subsequent to these procedures are apparently not appropriate to be categorized either as CA or HA infections, and hence they have been named health care-associated (HCA) infections.[4] Recent studies indicated that community-onset HCA infections are more similar to HA than to CA infections.[4,5] It also has been reported that the antimicrobial resistance among HCA-UTI pathogens is much higher than their counterparts associated with CA-UTI.[6–8] In Taiwan, although patients from the health care-associated settings are increasing, reports regarding the antimicrobial resistance in pathogens associated with HCA-UTI are rare. Still, some reports have indicated that community-onset infections in patients with prior hospitalization history or frequent hospital exposures, as well as those residing in nursing homes or referred from other health care facilities, were more likely to be associated with resistant microorganisms.[9,10]

The majority of CA-UTI (64.5-82%)[6–8,11] or uncomplicated UTI (75-95%)[2,12] are caused by *Escherichia coli*. Therefore, empirical antimicrobial therapy for the treatment of such infections is usually based on the local antimicrobial susceptibilities of this organism.[2] Even with complicated UTI, although the etiology may be complicated by the deficiency in host factors, *E. coli* remains the most frequent causative agent for such infections.[13] As to HCA-UTI or HA-UTI, although the reported bacterial spectra may differ in various studies, *E. coli* is still one of the most frequent pathogens.[6–8,11] Unfortunately, the organism is associated with an increasing antimicrobial resistance, thereby adding difficulties in the selection of appropriate agents for effective antimicrobial treatment.[14] To differentiate the antimicrobial susceptibilities associated with UTI of different origins of acquisition, i.e., CA-UTI, HCA-UTI, and HA-UTI, urinary isolates of *E. coli* were used as representatives and analyzed herein.

Materials and methods

The study was performed at a 622-bed regional hospital in southern Taiwan. In 2012, a total of 312 *E. coli* urinary isolates were identified. Antimicrobial susceptibilities were tested by a standard disk diffusion assay (Table 1). The results were interpreted according to the criteria suggested in 2012 by the Clinical Laboratory Standards Institute (CLSI).[15] However, according to a consensus statement made by several professional societies in Taiwan,[16] imipenem and meropenem results were interpreted by using the CLSI criteria suggested in 2009.[17] Extended-spectrum β-lactamase (ESBL) production among the isolates was also examined with the confirmatory method suggested by the CLSI without the change of cephalosporin susceptibility results.[17]

The cases were further categorized according to the following definitions. HA-UTI was defined if the case was identified after 4 or more days of hospitalization. Among the other non-HA-UTI cases, if the patients were residents

Table 1 Comparison of antimicrobial susceptibilities among urinary isolates of *Escherichia coli* and the proportions of extended-spectrum β-lactamase-producing isolates among various infection categories.

Antibiotics	Susceptibility (%)				p^*		
	All	CA	HCA	HA	CA vs.		HCA vs.
					HCA	HA	HA
	(n = 296)	(n = 85)	(n = 100)	(n = 106)			
Total isolates							
Cefazolin	25.7	49.4	13.0	18.9	<0.001	<0.001	NS
Cefuroxime	54.7	85.9	44.0	41.5	<0.001	<0.001	NS
Ceftriaxone	55.4	85.9	45.0	43.4	<0.001	<0.001	NS
Ceftazidime	56.8	87.1	47.0	44.3	<0.001	<0.001	NS
Ampicillin/sulbactam	40.5	71.8	32.0	25.5	<0.001	<0.001	NS
Imipenem	99.3	100.0	100.0	98.1	NS	NS	NS
Meropenem	99.3	100.0	99.0	99.1	NS	NS	NS
Gentamicin	63.5	75.3	59.0	60.4	<0.05	<0.05	NS
Amikacin	99.3	100.0	98.0	100.0	NS	NA	NS
Levofloxacin	44.9	68.2	33.0	38.7	<0.001	<0.001	NS
TMP/SMZ	43.2	55.3	37.0	38.7	<0.05	<0.05	NS
ESBL-producing isolates	26.0	3.5	30.0	34.9	<0.001	<0.001	NS

*Comparison by Chi-square test, with $p < 0.05$ indicating statistical significance.
CA = community-acquired; ESBL = extended-spectrum β-lactamase-producing; HA = hospital-acquired; HCA = health care-associated; NA = not available; NS = no statistical significance; TMP/SMZ = trimethoprim/sulfamethoxazole.

of any nursing home or long-term care facility, re-admitted within 90 days of discharge from a previous hospitalization for 2 or more days, or within 30 days before the onset of the UTI, the patients had indwelling urethral catheters, had undergone any invasive urinary procedure, had received hemodialysis or intravenous chemotherapy on an outpatient basis, or had received specialized nursing care at home by qualified health care providers, they would be categorized as HCA-UTI.[8,11] The other non-HA-UTI cases that did not fulfill the HCA-UTI criteria and were from patients residing in the general community were categorized as CA-UTI. Patients who were referred from another hospital, although they may belong to HA-UTI, were not included for further analysis in the present study.

All isolates or isolates in the respective subgroups were further examined for duplication. If multiple isolates were identified from the same patient during the same hospitalization period, only the first isolate was included for analysis. If more than one E. coli isolates were identified from the same specimen, the isolate with the higher antimicrobial resistance would be selected for study.

For statistical analysis, the Chi-square test was used. A difference was considered statistically significant when $p < 0.05$.

Results

A total of 296 nonrepetitive E. coli urinary isolates were analyzed (Table 1). High susceptibilities (>99%) were noted in imipenem, meropenem, and amikacin. Susceptibilities to other antimicrobial agents were all low at between 25.7% to cefazolin and 63.5% to gentamicin.

When the isolates were further subcategorized, similar conditions were found among isolates from the HA and HCA groups. By contrast, CA isolates were relatively more susceptible to the antibiotics tested, and high susceptibilities (>80%) could be noted in the second and third generation cephalosporins (cefuroxime, ceftriaxone, and ceftazidime), carbapenems (imipenem and meropenem), and amikacin. Although the high susceptibilities to carbapenems and amikacin were found in all groups, the susceptibilities to cefuroxime, ceftriaxone, and ceftazidime were significantly higher in CA isolates than in the others ($p < 0.001$). Furthermore, susceptibilities to other antibiotics, such as cefazolin, ampicillin/sulbactam, and levofloxacin, although only ranged between 49.4% and 71.8%, were also significantly higher in CA isolates than in the others ($p < 0.001$). For gentamicin and trimethoprim/sulfamethoxazole, the susceptibilities were also higher, although with a lower significance, when isolates from the CA group were compared with those from the HCA or HA groups ($p < 0.05$).

ESBL production was found in 26.0% of the isolates. Although the proportion of such isolates was similar between the HCA and HA isolates, a significantly lower proportion (3.5%) was noted in CA isolates ($p < 0.001$).

Discussion

Previous reports indicated that differences in the antimicrobial susceptibility patterns are present between CA-UTI/HCA-UTI[6,7] and between CA-UTI/HA-UTI.[3] A few recent studies also demonstrated the differences among clinical and microbiological characteristics in patients with CA-UTI, HCA-UTI, and HA-UTI.[8,11] In the present study, using E. coli urinary isolates as the representative, we further demonstrated that antimicrobial susceptibilities of HCA-UTI isolates were similar to those of HA-UTI isolates but were significantly lower than those of CA-UTI isolates. The results echoed the findings in a recent report[8] and suggested that despite the initial empirical antibiotic therapy, urine cultures for antimicrobial susceptibility testing are required, especially for HCA-UTI, to guide the subsequent definite antibiotic therapy.

In the present study, the majority of the patients in the HCA-UTI group were residents of nursing homes and patients re-admitted within 90 days of discharge from a previous hospitalization. Previous reports indicated that nursing home residents are usually associated with high age, various underlying illnesses, and immobility.[18] Compared to other community dwellers, hospital visits are relatively more frequent or sometimes inevitable among these patients.[18] Frequent hospitalization also provides the patients with close contact of the hospital environment. Consequently, when an infection, such as UTI, occurs, the associated pathogens may be more likely to be related to hospitals, that is, HAI pathogens, although the patients are not hospitalized at the onset of the infection. Under such circumstances, the appropriate empirical antimicrobial agents should be similar for HCA-UTI and HA-UTI patients. However, without such awareness, HCA-UTI would likely be treated as CA-UTI because the patients were literally from a nonhospital environment. Failure in clinical recognition may lead to inadequate antibiotic therapy,[19] especially for the treatment of severe complicated HCA-UTI, and the subsequent adverse outcomes may be expected.[20] Therefore, patients with HCA-UTI should be differentiated from those with CA-UTI, and accordingly, the antimicrobial susceptibilities of HCA-UTI isolates should be analyzed independently.

In consistence with a consensus review of the epidemiology and appropriate antimicrobial therapy of complicated UTI in Asia-Pacific region,[1] data on CA-UTI in our hospital support the view that care should be taken when using trimethoprim/sulfamethoxazole or fluoroquinolones for empirical treatment of CA-UTI, particularly complicated CA-UTI in moderately to severely ill patients. Furthermore, empirical antibiotics for the treatment of serious complicated UTIs in which risk factors for resistant organisms exist should include broad-spectrum antibiotics, such as imipenem or meropenem.

In conclusion, using E. coli as the representative organism, the present study demonstrated the differences in antimicrobial susceptibilities among CA-UTI, HCA-UTI, and HA-UTI isolates. Clinicians should be aware that non-HA-UTI in patients who have frequent health care contacts, i.e., HCA-UTI, is likely to be associated with higher antimicrobial resistance similar to those observed in HA-UTI. Furthermore, considerable variability in the antimicrobial susceptibility patterns may also exist among the frequent pathogens of various infections, in different patient populations, and from diverse institutions. Local antimicrobial susceptibility patterns are therefore critical and should be established respectively for the effective management of

HCA-UTI. Although clinical severity should also be considered when prescribing empirical antibiotics, urine cultures for susceptibility testing are still required, especially for HCA-UTI patients, to guide the subsequent definite antibiotic therapy.

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