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Original Article

In vitro activities of 16 antimicrobial agents against clinical isolates of extended-spectrum beta-lactamase-producing *Escherichia coli* and *Klebsiella pneumoniae* in two regional hospitals in Taiwan

Chun-Hsing Liao[1], Wang-Huei Sheng[1], Jann-Tay Wang[1], Hsin-Yun Sun[1], Hua-Kung Wang[2], Po-Ren Hsueh[3], Yee-Chun Chen[1], Shan-Chwen Chang[1]

[1]Department of Internal Medicine, National Taiwan University Hospital, Taipei; [2]Department of Internal Medicine, En-Chu-Kong Hospital, Taipei; and [3]Department of Laboratory Medicine, National Taiwan University Hospital, Taipei, Taiwan

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Background and Purpose: Infections due to extended-spectrum beta-lactamase (ESBL)-producing *Escherichia coli* and *Klebsiella pneumoniae* (ESBL-EC and ESBL-KP) have become an important clinical problem. Local knowledge of antimicrobial susceptibilities of these organisms is important for implementation of effective hospital anti-infective policies.

Methods: We analyzed the activities of various antimicrobial agents against recent isolates of ESBL-EC and ESBL-KP from 2 regional hospitals using the agar dilution method to determine minimal inhibitory concentrations (MICs). A total of 80 strains of ESBL-EC and 101 strains of ESBL-KP collected during 2003 and 2004 were included in the study.

Results: The MICs of all carbapenems were relatively low, with almost all isolates being susceptible. In contrast, only 30.0% of ESBL-EC and 36.6% of ESBL-KP were susceptible to ciprofloxacin. Flomoxef and cefmetazole were the most active cephamycins (88.8% and 90.0% ESBL-EC and 93.1% and 87.1% ESBL-KP susceptible, respectively), followed by ceftibuten (85.0% and 80.2%) and cefoxitin (42.5% and 49.5%). A cefepime MIC ≤8 mg/L was found in 77.5% of ESBL-EC and 73.3% of ESBL-KP isolates. The susceptible rates to amikacin and isepamicin were both 81.3% for ESBL-EC; 72.3% and 73.3% for ESBL-KP. Inter-hospital differences in susceptibilities were demonstrated for several antimicrobials.

Conclusions: The inter-hospital variation of these data emphasizes the need for monitoring of antimicrobial susceptibility profiles at the individual hospital level and to establish rationales supporting policy for treating infections caused by ESBL-producing bacteria.

Key words: Aminoglycosides, beta-lactamases, carbapenems, cephalosporins, cephamycins, fluoroquinolones

Introduction

The emergence of extended-spectrum beta (β)-lactamase (ESBL)-producing *Escherichia coli* and *Klebsiella pneumoniae* (ESBL-EC and ESBL-KP) may be associated with a reduced set of therapeutic alternatives [1-6]. ESBL confers the ability to hydrolyze broad-spectrum oxymino-β-lactams and confers resistances to these agents, but has no activity against carbapenems and cephamycins [1-3]. Carbapenems are the most reliable agents in improving the survival rate of patients with ESBL-KP bacteremia [3,6,7]. However, indiscriminate use of carbapenems could promote carbapenem resistance [8]. Besides, a recent study reported that delaying appropriate definitive antimicrobial therapy for patients infected with ESBL-producing strains before acknowledging the final identification is not associated with a higher mortality [9]. Thus,

Corresponding author: Shan-Chwen Chang, Department of Internal Medicine, National Taiwan University Hospital, 7 Chung-Shan South Road, Taipei, Taiwan.
E-mail: sc4030@ha.mc.ntu.edu.tw

identification of alternative agents which may be used as empirical or specific therapy for suspected or confirmed infection caused by ESBL producers is crucial for the provision of therapeutic options and to limit the spread of resistance.

Ciprofloxacin has been recommended as an alternative in treating infections caused by ESBL producers [10], but a variety of in vitro resistances have subsequently been widely reported [6,11-15]. The roles of other antimicrobials with potential activity against ESBL-producing *Enterobacteriaceae* — such as fourth-generation cephalosporins, cephamycins, and aminoglycosides — remain controversial. One study suggested that the minimal inhibitory concentration (MIC) of cefepime can be used as a predictor for the type of ESBL in ESBL-KP and also as a guide for clinical use [16]. On the other hand, a high percentage of aminoglycoside resistance among ESBL-KP isolates has also been reported [15].

The role of cephamycins against ESBL-producing isolates has also long been questioned [6,17-19]. Ceftibuten, an oral cephamycin, was recently reported to retain activity against ESBL-EC, except those producing SHV-4, SHV-5 and SHV-12 [20]. Furthermore, new carbapenems, such as ertapenem [21] and panipenem [22] have good activities against ESBL producers but are less active against *Pseudomonas aeruginosa*.

This study analyzed the *in vitro* activities of various antibacterial agents against clinical isolates of ESBL-EC and ESBL-KP. The analysis included 80 isolates of ESBL-EC and 101 isolates of ESBL-KP collected from 2 regional hospitals in Taiwan. MICs were determined for 16 different antimicrobial agents. The goal of this study was to evaluate the potential of these agents as alternatives for specific therapy in confirmed infection caused by ESBL producers. The discrepancy of antimicrobial susceptibility patterns between the 2 regional hospitals was also compared, and pulsed-field gel electrophoresis (PFGE) was performed in selected isolates to identify whether clustering of those ESBL producers existed [13].

Methods

Bacterial isolates

ESBL-EC and ESBL-KP isolates were collected consecutively in 2003 and 2004 from En-Chu-Kong Hospital (ECKH; a regional hospital in Taipei County) and Yun-Lin Hospital (YLH; a regional hospital in Yun-Lin County). The bacteria were isolated from various clinical specimens and from both outpatients and inpatients treated in various departments and wards of the hospitals. Duplicate patient isolates were excluded. Double disk confirmatory tests [23] were performed using cefotaxime, cefotaxime-clavulanate, ceftazidime, and ceftazidime-clavulanate to confirm the ESBL phenotype. Isolates displaying positive double disk synergy were considered ESBL producers.

Antimicrobial susceptibility testing

MICs were determined by the agar dilution method [24]. Briefly, 10^4 colony-forming units of bacteria were inoculated onto the Mueller-Hinton agar plates, which contained a series of 2-fold dilutions of tested antimicrobial agents, using a Steers' replicator. After incubation at 35°C for 18-20 h, MICs were identified according to the lowest concentration of the antimicrobial agent that completely inhibited the growth of bacteria on the agar plate.

For antimicrobial agents without established MIC determination criteria, the following breakpoints were used: the breakpoint of imipenem was used as an indicator for panipenem; the breakpoint of moxalactam was used for flomoxef; the breakpoint of amikacin was used for isepamicin. These criteria are summarized in Table 1. The concentration of antimicrobial agents ranged from 0.03 mg/L to 128 mg/L. *E. coli* American Type Culture Collection [ATCC] 25922 and *E. coli* ATCC 35218 were used as the internal control strains.

The tested antimicrobial agents were ciprofloxacin (Bayer Co., West Haven, CT, USA); meropenem (Sumitomo Pharmaceuticals, Osaka, Japan); cefepime and amikacin (Bristol-Myers Squibb, Princeton, New Jersey, USA); imipenem, ertapenem and cefoxitin (Merck, Sharp and Dohme, Rahway, New Jersey, USA); flomoxef and ceftibuten (Shionogi and Co., Ltd, Osaka, Japan); cefotaxime (Marion Merrell Dow, Cincinnati, OH, USA); panipenem (Kirin, Tokyo, Japan); cefpodoxime and cefmetazole (Sankyo,

Table 1. The proposed minimal inhibitory concentration (MIC) interpretation criteria for antimicrobial agents without National Committee for Clinical Laboratory Standards criteria

Antimicrobial agent	MIC value (mg/L)		
	Susceptible	Intermediate	Resistant
Panipenem	≤4	8	≥16
Flomoxef	≤8	16-32	≥64
Isepamicin	≤16	32	≥64

Tokyo, Japan); cefixime (Fujisawa, Osaka, Japan); gentamicin (Schering Plough, Bloomfield, New Jersey, USA); and isepamicin (TTY Biopharm, Taipei, Taiwan).

Statistical analysis

We compared the differences in susceptibility of ESBL-EC and ESBL-KP isolates from 2 regional hospitals to 16 antimicrobials using chi-squared or Fisher's exact tests. Data were collected in a Microsoft Excel database (Microsoft Excel 2001; Microsoft Corporation, Seattle, WA, USA) and analyzed with Statistical Package for the Social Sciences (SPSS) software for Windows (Release 10.0; SPSS, Inc., Chicago, IL, USA).

Pulsed-field gel electrophoresis

PFGE was performed for selected isolates to delineate the molecular epidemiological characteristics of ESBL-producing bacterial isolates. The details of the method used for PFGE were described in our previous study [25]. For restriction endonuclease digestion of the DNA plug, *Xba*I was used for ESBL-KP isolates and *Not*I for ESBL-EC isolates. Other procedures were as described in our previous study [25]. The PFGE results were analyzed with Gelcompar for Windows Version 3.1. Band pattern similarity above 80% was considered as a probable cluster [26].

Results

A total of 80 strains of ESBL-EC (48 from YLH and 32 from ECKH), and 101 strains of ESBL-KP (44 from YLH and 57 from ECKH) were collected. The MICs of different antimicrobials for ESBL-EC are shown in Table 2. All isolates were susceptible to carbapenems (MIC range, <0.03-4 mg/L). The susceptible rate to ciprofloxacin was 30.0% (MIC for 90% of isolates [MIC_{90}], 64 mg/L; range, <0.03->128 mg/L). The MIC_{90} of cephamycins included 16 mg/L for flomoxef (range, <0.03-64 mg/L; susceptible rate, 88.8%), 16 mg/L for cefmetazole (range, 0.5->128 mg/L; susceptible rate, 90.0%), 32 mg/L for cefoxitin (range, 2->128 mg/L; susceptible rate, 42.5%), and 64 mg/L for ceftibuten (range, 0.06->128 mg/L; susceptible rate, 85.0%). For cefepime, an MIC ≤8 mg/L was found in 77.5% of strains, and the MIC_{90} was 16 mg/L. For aminoglycosides, although the MIC_{90} of the 3 agents tested was >128mg/L, susceptibility to gentamicin was found in 18.8% (range, 0.25->128 mg/L), in contrast with 81.3% to amikacin (range, 0.5->128 mg/L) and 81.3% to isepamicin (range, 0.25->128 mg/L).

The MICs of different antimicrobials for ESBL-KP are shown in Table 2. All but 1 of the isolates were susceptible to carbapenems (MIC range, <0.03-8 mg/L; susceptible rate, ≥99%).One isolate had an MIC of

Table 2. Antimicrobial susceptibilities of 80 clinical isolates of extended-spectrum beta-lactamase (ESBL)-producing *Escherichia coli* and *Klebsiella pneumoniae* to 16 drugs

	ESBL-producing *E. coli*						ESBL-producing *K. pneumoniae*					
	MIC (mg/L)			S (%)	I (%)	R (%)	MIC (mg/L)			S (%)	I (%)	R (%)
	50%	90%	Range				50%	90%	Range			
Imipenem	0.5	1	0.125-4	100.0	0	0	0.5	1	0.125-2	100.0	0	0
Meropenem	<0.03	0.06	<0.03-0.125	100.0	0	0	0.06	0.125	<0.03-2	100.0	0	0
Ertapenem	<0.03	0.25	<0.03-1	100.0	0	0	0.125	0.5	0.06-8	99.0	0	1.0
Panipenem	0.25	0.5	0.06-4	100.0	0	0	0.25	0.5	0.06-2	100.0	0	0
Cefepime[a]	4	16	0.06-32	-	-	-	4	32	0.25-128	-	-	-
Cefotaxime[a]	32	64	0.125-128	-	-	-	32	128	2->128	-	-	-
Cefixime	8	128	0.5->128	-	-	-	32	>128	0.25->128	-	-	-
Cefpodoxime	128	>128	0.5->128	-	-	-	64	>128	8->128	-	-	-
Flomoxef	0.5	16	<0.03-64	88.8	10.0	1.2	0.5	4	0.06-64	93.1	5.9	1.0
Cefmetazole	8	16	0.5->128	90.0	5.0	5.0	8	32	0.5->128	87.1	5.0	7.9
Cefoxitin	16	32	2->128	42.5	45.0	12.5	16	32	2->128	49.5	28.7	21.8
Ceftibuten	1	64	0.06->128	85.0	2.5	12.5	4	32	0.06->128	80.2	7.9	11.9
Ciprofloxacin	32	64	<0.03->128	30.0	0	70.0	8	64	<0.03-128	36.6	6.0	57.4
Gentamicin	64	>128	0.25->128	18.8	6.2	75.0	32	>128	0.25->128	15.8	13.9	70.3
Amikacin	2	>128	0.5->128	81.3	0	18.7	8	>128	0.5->128	72.3	1.0	26.7
Isepamicin	1	>128	0.25->128	81.3	0	18.7	1	>128	0.06->128	73.3	0	26.7

Abbreviations: MIC = minimal inhibitory concentration; S = susceptible; I = intermediate; R = resistant

[a]All ESBL producers should be designated as resistant to cefepime, cefotaxime, cefixime and cefpodoxime.

8 mg/L for ertapenem. Ciprofloxacin susceptibility was found in 36.6% of isolates (MIC_{90}, 64 mg/L; range, <0.03->128 mg/L). The MIC_{90} of cephamycins included 4 mg/L for flomoxef (range, 0.06-64 mg/L; susceptible rate, 93.1%), 32 mg/L for cefmetazole (range, 0.5->128 mg/L; susceptible rate, 87.1%), 32 mg/L for cefoxitin (range, 2->128 mg/L; susceptible rate, 49.5%) and 32 mg/L for ceftibuten (range, 0.06->128 mg/L; susceptible rate, 80.2%). For cefepime, an MIC ≤8 mg/L was found in 73.3% of strains, but the MIC_{90} was 32 mg/L. For aminoglycosides, although the MIC_{90} values of the 3 agents tested were all >128 mg/L, susceptibility to gentamicin was found in 15.8% (range, 0.25->128 mg/L), in contrast with 72.3% to amikacin (range, 0.5->128 mg/L) and 73.3% to isepamicin (range, 0.06->128 mg/L).

Comparison of the susceptibilities of ESBL-EC isolates between the 2 regional hospitals (Table 3) revealed lower susceptible rates to ciprofloxacin for isolates from YLH (20.8% versus 50.0%). Additionally, the MIC_{90} of amikacin and isepamicin for the isolates from ECKH was 2 mg/L and 1 mg/L, respectively, but was >128 mg/L for both of these antibiotics in isolates from YLH. Conversely, the MICs of cephamycins for isolates from YLH were generally lower than those from ECKH, except for cefoxitin. Comparison of susceptibility profiles of ESBL-KP isolates from the 2 hospitals is also shown in Table 3. A lower susceptible rate to ciprofloxacin was found in isolates from YLH (15.9% versus 42.1%). In addition, ESBL-KP isolates had a lower susceptible rate to cefoxitin than isolates from ECKH (19.3% versus 88.6%).

The differences of aminoglycoside activity for ESBL-EC between the 2 hospitals were further investigated to determine clonicity. All 13 ESBL-EC isolates from YLH with high-level amikacin resistance (i.e., MIC >128mg/L) were examined by PFGE, which revealed 2 clusters (isolate B, E, F as one group and isolate I, J as the other group) and implied the existence of nosocomial spreading (Fig. 1). Part of the PFGE results for these isolates are shown in Fig. 1A. In comparison, analysis of the 12 ESBL-KP isolates from the YLH with amikacin MIC above 128 mg/L was also examined by PFGE, which revealed no clustering (Fig. 1B).

Discussion

Emergence of ESBL-producing *Enterobacteriaceae* has been reported since 1983 in many countries, including

Table 3. Comparison of MIC_{90} of extended-spectrum beta-lactamase (ESBL)-producing *Escherichia coli* and *Klebsiella pneumoniae* between 2 regional hospitals

	ESBL-producing *E. coli*						ESBL-producing *K. pneumoniae*					
	Isolates from En-Chu-Kong Hospital (n = 32)			Isolates from Yun-Lin Hospital (n = 48)			Isolates from En-Chu-Kong Hospital (n = 57)			Isolates from Yun-Lin Hospital (n = 44)		
	MIC_{90} (mg/L)	Range (mg/L)	S (%)	MIC_{90} (mg/L)	Range (mg/L)	S (%)	MIC_{90} (mg/L)	Range (mg/L)	S (%)	MIC_{90} (mg/L)	Range (mg/L)	S (%)
Imipenem	0.5	0.125-2	100.0	1	0.125-4	100.0	1	0.5-1	100.0	1	0.125-2	100.0
Meropenem	0.06	<0.03-0.06	100.0	0.06	<0.03-0.125	100.0	<0.03	<0.03-2	100.0	0.06	<0.03-0.25	100.0
Ertapenem	0.25	<0.03-1	100.0	0.25	<0.03-0.5	100.0	0.25	<0.03-8	98.2	0.25	<0.03-1	100.0
Panipenem	0.25	0.06-0.5	100.0	1	0.125-4	100.0	0.5	0.25-2	100.0	0.25	0.06-1	100.0
Cefepime[a]	16	0.125-32	-	16	0.06-32	-	16	0.25-64	-	16	0.5-128	-
Cefotaxime[a]	64	2-128	-	64	0.125-128	-	128	2->128	-	128	2->128	-
Cefixime	>128	1->128	-	32	0.5-128	-	>128	1->128	-	64	2->128	-
Cefpodoxime	>128	8->128	-	>128	0.5->128	-	>128	16->128	-	128	8->128	-
Flomoxef	16	<0.03-64	71.9	0.5	0.25-8	100.0[b]	8	0.25-32	89.5	1	0.06-64	97.7
Cefmetazole	32	0.5->128	75.0	8	1-16	100.0[b]	64	4-128	82.5	8	0.5->128	93.2
Cefoxitin	64	2->128	59.4	16	4-16	31.3[b]	64	4->128	19.3	64	2->128	88.6[b]
Ceftibuten	128	0.125->128	65.6	4	0.06-16	97.9[b]	32	0.125->128	77.2	16	0.25-64	86.4
Ciprofloxacin	64	<0.03-128	50.0	64	<0.03->128	20.8[b]	64	0.06-128	42.1	128	0.06-128	15.9[b]
Gentamicin	64	0.25->128	31.3	>128	0.5->128	10.4[b]	>128	0.5->128	19.3	>128	0.25->128	11.4
Amikacin	2	0.5->128	96.9	>128	0.5->128	70.8[b]	>128	2->128	71.9	>128	0.5->128	75.0
Isepamicin	1	0.25->128	96.9	>128	0.5->128	70.8[b]	>128	1->128	71.9	>128	0.06->128	75.0

Abbreviations: MIC_{90} = minimal inhibitory concentration for 90% of isolates; S = susceptible

[a]All ESBL producers should be designated as resistant to cefepime, cefotaxime, cefixime and cefpodoxime.

[b]$p<0.05$.

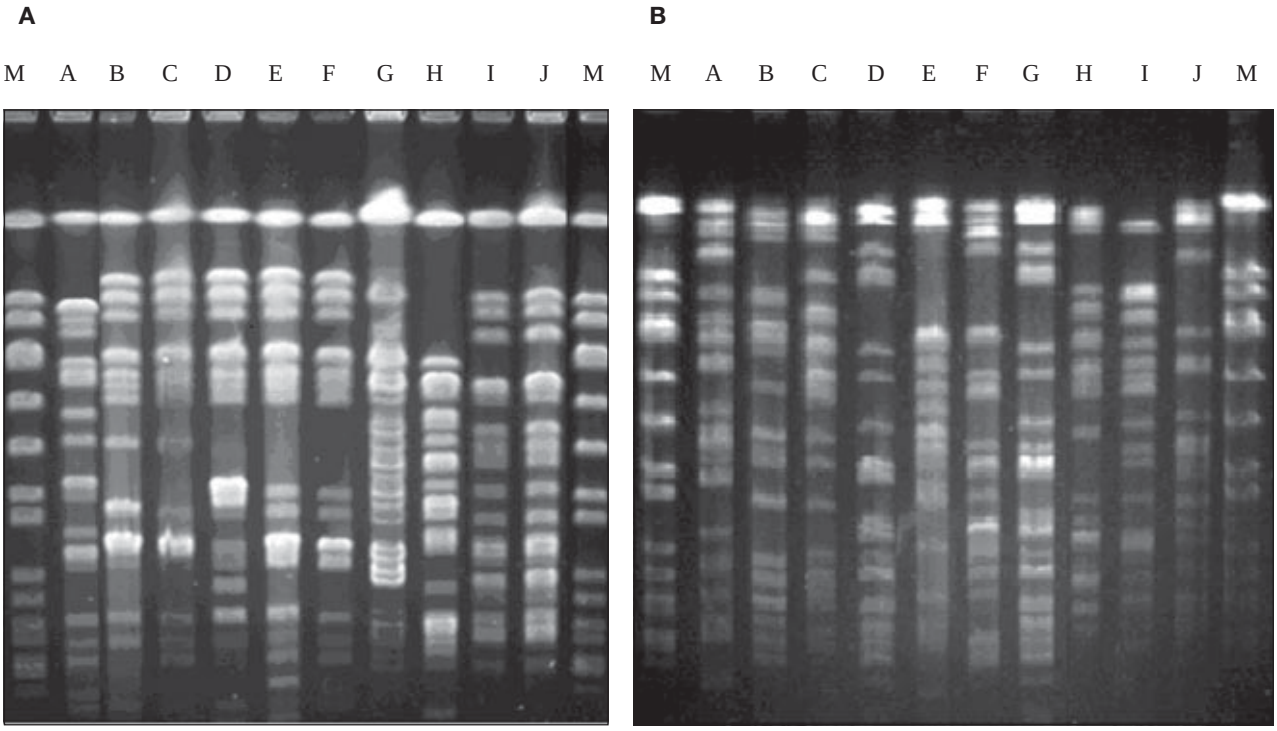

Fig. 1. Pulsed-field gel electrophoresis of extended-spectrum beta-lactamase (ESBL)-producing *Escherichia coli* and *Klebsiella pneumoniae* isolates with high amikacin minimal inhibitory concentrations from Yun-Lin Hospital. A) Ten isolates of ESBL-producing *E. coli*. Isolates B, E and F, and isolates I and J, are clustered. B) Ten isolates of ESBL-producing *K. pnuemoniae* showing no obvious clustering.

Taiwan [6,13,15,27-29]. The treatment options for infections due to ESBL-producing strains include carbapenems, fluoroquinolones, and other antimicrobial agents with in vitro activity, such as cephamycins, fourth-generation cephalosporins, β-lactam/β-lactamase inhibitors and aminoglycosides [3,10]. In the present study, carbapenems exhibited satisfactory activity against ESBL-producing bacterial strains in the 2 regional hospitals. Cephamycins, fourth-generation cephalosporins, and the newer generation of aminoglycosides (amikacin and isepamicin) showed variable activity against ESBL-EC and ESBL-KP. High rates of fluoroquinolone resistance were observed for ESBL-EC and ESBL-KP, however, negating their role as an alternative empirical agent.

Among the carbepenems, ertapenem has been reported to have minimal selectivity for *P. aeruginosa* mutants with cross-resistance to imipenem under clinical conditions [30]. Given its excellent MIC values and minimal selectivity, ertapenem appears to be a good candidate for treating patients with infection caused by ESBL producers. Panipenem, which has limited activity against *P. aeruginosa* [31], may possess a similar role to ertapenem.

Fluoroquinolones have been suggested as alternative agents for the treatment of infections caused by ESBL producers [10]. Data from the Surveillance from Multicenter Antimicrobial Resistance in Taiwan (SMART) program indicated the resistance rate to ciprofloxacin among *E. coli* ranged from 11% to 33%, while in *K. pneumoniae* it ranged from 5% to 33% [5]. The ciprofloxacin resistance rate of ESBL-KP and ESBL-EC has been reported in the range from 18% to 55% [5,6,11-13]. By comparison, in the present study, the susceptibility rates to ciprofloxacin for ESBL-EC and ESBL-KP (30.0% and 36.6%, respectively) were much lower than in previous studies [6,13]. Widespread use of fluoroquinolones [32-33] and clonal spreading [13] has resulted in the emergence of fluoroquinolone resistance at a rapid rate. The high prevalence of fluoroquinolone resistance among ESBL-EC and ESBL-KP isolates in this study suggests that a fluoroquinolone is no longer a suitable alternative agent for empirical treatment in patients with infections suspected to be due to ESBL producers in these 2 hospitals.

Although ESBLs derived from TEM and SHV β-lactamases do not confer resistance to cephamycins, Jacoby et al found that over half of *E. coli* and 29% of

K. pneumoniae isolates tested by disk diffusion were resistant to cefoxitin. [17]. Jean et al found that the susceptibility of cefotaxime-resistant *E. coli* to cefoxitin and flomoxef was 26% and 61%, while those of cefotaxime-resistant *K. pnuemoniae* was 57% and 84% [6]. In the present study, the susceptibility rates to flomoxef and cefmetazole were around 90% for both ESBL-EC and ESBL-KP, and those to ceftibuten, the oral cephamycin, were above 80%. However, the rate of susceptibility to cefoxitin was lower. Despite the fact that the results of MICs of flomoxef and cefmetazole were within the therapeutic range, the in vivo selection of a cephamycin-resistant, porin-deficient mutant of *K. pneumoniae* producing a TEM-3 β-lactamase has been reported [18]. On the other hand, a more recent case report demonstrated successful treatment of ESBL-KP peritonitis with intraperitoneal flomoxef [19]. Thus, the clinical role of cephamycins for ESBL-producing bacteria may vary and requires continued monitoring; the low MICs of these agents make them potential therapeutic candidates.

Whether fourth-generation cephalosporins remain alternatives for treatment of infection caused by ESBL producers remains controversial when the decision is based on disk test results showing susceptibility because of the inoculum effect [16,28-29,34-36]. However, the clinical use of cefepime is not advised when MIC exceeded 8 mg/L, as this predicts the presence of CTX-M β-lactamases; by contrast, cefepime can be used with confidence if the MIC is less than 1 mg/L [16]. In the present study, the MIC_{90} of cefepime for ESBL-KP exceeded 8 mg/L, even when the MIC for 50% of isolates (MIC_{50}) was above the level within which cefepime could be used reliably. Overall, 23.8% of ESBL-EC and 15.8% of ESBL-KP had cefepime MIC ≤1 mg/L. These results suggest the need for cautious use of cefepime in the treatment of ESBL-KP infections, especially for severe infections in these hospitals.

Aminoglycosides showed variable activities in previous studies [6,15]. Yu et al reported 96% of ESBL-KP were resistant to both gentamicin and tobramycin, and 62% to amikacin [15]. Nevertheless, Jean et al found that the amikacin resistance rates in cefotaxime-resistant *E. coli* and *K. pneumoniae* were 15% and 28%, respectively [6]. In this study, the MICs of amikacin and isepamicin were significantly lower than gentamicin. ESBL-EC isolates from ECKH had MIC_{90} for these agents which were well within the therapeutic range. These results indicate that amikacin and isepamicin can be considered as alternative agents, or be incorporated into combination therapy in these hospital settings.

The comparison of ESBL-producing isolates between the 2 regional hospitals in this study revealed clinically important inter-hospital differences. Fluoroquinolone resistance rates are high in both hospitals, especially for isolates from YLH. Additionally, in the comparison of ESBL-EC, higher aminolycoside and lower cephamycin resistance, except for cefoxitin, was demonstrated for isolates from YLH. PFGE revealed 2 clusters among isolates with high amikacin MICs from YLH. As for the exceptionally low activity of cefoxitin among ESBL-KP isolates from ECKH, most of the non-susceptible isolates (66.7%) had MICs in the range of 16 and 32 mg/L.

In summary, among the isolates collected from the 2 regional hospitals, carbapenems remain the most active agents against ESBL-EC and ESBL-KP. Cephamycins, especially flomoxef and cefmetazole, could be considered as alternative antimicrobials for patients infected with ESBL-EC and ESBL-KP. Rapid evolution of fluoroquinolone resistance might decrease the clinical utility of this agent. As to fourth-generation cephalosporins, despite the fair percentage of isolates with MIC ≤8 mg/L, the relatively high MIC levels should be taken into consideration. Some aminoglycosides, such as amikacin and isepamicin, could be considered for use in combination with β-lactams against resistant bacteria. Finally, inter-hospital differences in antimicrobial resistances could be prominent; thus, it is important for every hospital to establish its own susceptibility profile and to use this information to propose a rationale for treating infections caused by ESBL producers.

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