KJU
Korean Journal of Urology

www.kjurology.org
http://dx.doi.org/10.4111/kju.2014.55.4.270

Original Article - Infection/Inflammation

Clinical Efficacy of Ertapenem for Recurrent Cystitis Caused by Multidrug-Resistant Extended-Spectrum β-Lactamase-Producing *Escherichia coli* in Female Outpatients

Sungmin Song, Chulsung Kim, Donghoon Lim

Department of Urology, Chosun University School of Medicine, Gwangju, Korea

Purpose: To evaluate the clinical outcomes of ertapenem administered as an outpatient parenteral antibiotic therapy for intractable cystitis caused by extended-spectrum β-lactamase (ESBL)-producing *Escherichia coli*.

Materials and Methods: We retrospectively reviewed a case series of 3 years of therapeutic experience with ertapenem for intractable recurrent cystitis caused by ESBL-producing *E. coli*. Ertapenem 1 g/d was parenterally administered to the patients on an outpatient basis until the acquisition of symptomatic improvement and negative conversion of urine culture. Demographic and clinical characteristics of patients, antimicrobial resistance, and clinical response data were analyzed from the patients' medical records.

Results: During the course of this study, a total of 383 patients were diagnosed with cystitis, and 24 of them showed ESBL-producing *E. coli* (6.26%). The mean treatment duration of all patients was 8.5 days. The early clinical and microbiological cure rates 0 to 7 days after the end of treatment were 91.7% (22/24) and 90.9% (20/22), respectively. The late clinical and microbiological cure rates 4 to 6 weeks after the end of treatment were 72.2% (13/18) at both time points.

Conclusions: Parenteral ertapenem treatment can be an effective and well-tolerated treatment option for intractable recurrent cystitis by multidrug-resistant ESBL-producing *E. coli*.

Keywords: *Bacterial multiple drug resistance; Beta-lactams; Cystitis; Ertapenem; Escherichia coli*

Article History:
received 9 September, 2013
accepted 16 October, 2013

Corresponding Author:
Donghoon Lim
Department of Urology, Chosun University Hospital, Chosun University School of Medicine, 365 Pilmun-daero, Dong-gu, Gwangju 501-717, Korea
TEL: +82-62-220-3210
FAX: +82-62-232-3210
E-mail: dhlim@chosun.ac.kr

INTRODUCTION

Urinary tract infections (UTIs) are very common bacterial infections, with a global incidence of over 250 million cases per year [1]. Most UTIs are uncomplicated infections in women. About one-third of all women may have at least one episode of uncomplicated cystitis in their lifetime [2]. In clinical practice, uncomplicated cystitis is usually managed with empirical oral antimicrobials on an outpatient basis, because the causative microorganism is generally predictable in healthy women [3].

Extended-spectrum β-lactamases (ESBLs), which can be produced by *Enterobacteriaceae*, are enzymes that can confer resistance to most β-lactam antibiotics. The incidence of infection with ESBL-producing bacteria has been increasing worldwide [4]. ESBL-producing bacteria typically show cross-resistance to fluoroquinolones and other antimicrobial agents, and therefore, the choice of the appropriate empirical therapeutic regimen may be challenging. Intractable recurrent cystitis caused by ESBL-producing *Escherichia coli* is considered a complicated UTI. In this setting, patients may have persistent symptoms and unresolved or persistent bacteriuria, despite empirical oral antibiotic treatments [5,6]. Parenteral

carbapenem has recently been considered as the treatment of choice for ESBL-producing bacterial infections [7,8]. Therefore, patients should be in a hospital to complete their antibiotic therapy, even if they are clinically stable and ambulatory, which results in increased costs and length of stay.

Hence, we examined the clinical and microbiological outcomes associated with outpatient ertapenem therapy among female patients with community-acquired cystitis due to ESBL-producing *E. coli* and in whom empirical oral antibiotic therapy had failed. To our knowledge, this is the first study on the use of ertapenem to treat cystitis in female patients with failed empirical treatments owing to ESBL-producing *E. coli*.

MATERIALS AND METHODS

We retrospectively reviewed 24 cases of female cystitis caused by ESBL-producing *E. coli* and treated by once daily ertapenem injection therapy between January 2010 and December 2012. The demographic and clinical characteristics of the patients, including complicating risk factors, any antibiotics used in the past 6 months, the empirical antibiotics used to treat this episode, the treatment duration of ertapenem, clinical outcomes, microbiological outcomes, and antibiotic susceptibility, were analyzed from the patients' medical records. Our study and research were done in accordance with the ethical standards of the Institutional Review Board of the author's institute and with the Helsinki Declaration.

All patients had lower urinary tract symptoms (LUTS), pyuria (>5/high power field in the urine analysis), and culture-proven ESBL-producing *E. coli* in the urine ($>10^5$ colony-forming units/mL). Patients with systemic symptoms such as leukocytosis, flank pain, and fever; patients requiring hospitalization owing to limited mobility; and patients with chronic indwelling catheters were excluded from this study. The identification of the strains and the antimicrobial susceptibility test were conducted by using the Vitek II system (bioMerieux, Durham, NC, USA).

Ertapenem (Invanz) 1 g/d was parenterally administered to the patients on an outpatient basis until the acquisition of symptomatic improvement and negative conversion of urine culture. Patents were asked to report their symptoms every day. Follow-up urine culture was done when the patients became asymptomatic and near 1 week after the start of treatment. When the patients still had remnant symptoms or positive urine culture results 7 days after the initial treatment, we maintained the treatment for the next 7 days while waiting for the acquisition of symptomatic improvement and negative conversion of urine culture.

Clinical and microbiological outcomes were assessed twice: within 7 days (early) and 4 to 6 weeks (late) after the end of therapy, respectively. Clinical cure was defined as disappearance of the LUTS and microbiological cure was defined as a sterile urine culture.

To compare the groups with and without complicating risk factors, statistical analyses were performed by use of the Fisher exact test and Mann-Whitney U test based on IBM SPSS ver. 18.0 (IBM Co., Armonk, NY, USA). Values of $p<0.05$ were considered significant.

RESULTS

During the course of this study, a total of 383 patients were diagnosed with cystitis, and 24 of them showed ESBL-producing *E. coli* (6.26%). In terms of the antibiotic susceptibility pattern of the ESBL-producing *E. coli*, only one subject (4.5%) showed susceptibility to fluoroquinolone, and all the subjects (100%) showed susceptibility to amikacin and carbapenem. Fourteen isolates (63.6%) were susceptible to amoxicillin/clavulanate, which had the highest coverage among the oral agents (Table 1).

Table 2 displays the characteristics of ertapenem treatment for recurrent cystitis caused by ESBL-producing *E. coli*. The mean age of the 24 female patients was 47.1 years (range, 22–76 years). Thirteen had complicating risk factors, the most common of which were diabetes (n=5, 20.8%), urological operation and kidney transplantation (n=4, 16.7%), and neurologic disease (Parkinson disease) and short-term Foley catheter indwelling (n=1, 4.2%). Eleven patients did not have complicating factors. When the 13 patients who had complicating factors and the 11 patients who did not were compared, no significant differences were observed in their early clinical outcomes (100% vs. 84.6%, p=0.482), microbiological outcomes (100% vs. 66.7%, p=0.481), or mean treatment duration (8.1±3.5 days vs. 8.9±3.5 days, p=0.093).

The most frequently used antibiotic in the past 6 months was ciprofloxacin (n=21, 87.5%), third-generation cepha-

TABLE 1. Antibiotic susceptibility patterns of ESBL-producing *Escherichia coli*

Antimicrobial	No. of susceptible isolates (%)
Oral agent available	
TMP/SMX	6/22 (27.2)
Quinolone	1/22 (4.5)
Ciprofloaxcin	1/13 (7.7)
Levofloxacin	0/9 (0)
Amoxicillin/clavulanate	14/22 (63.6)
Ampicillin	0/22 (0)
Parenteral agents only	
Carbapenem	22/22 (100)
Imipenem	22/22 (100)
Meropenem	13/13 (100)
Ertapenem	9/9 (100)
Ceftazidime	0/22 (0)
Cefotaxim	0/22 (0)
Piperacillin/tazobactam	11/22 (50.0)
Amikacin	22/22 (100)

ESBL, extended-spectrum β-lactamases; TMP/SMX, trimethoprim/sulfamethoxazole.

TABLE 2. Treatment variables in patients receiving ertapenem for recurrent cystitis caused by ESBL-producing *Escherichia coli*

Patient	Age (y)	Complicating factors	Used antibiotics prior to ertapenem within 6 months (d)	Used empirical antibiotics to treat this episode (d)	Subdivision of causes of recurrence	Treatment duration of ertapenem (d)	Early clinical outcome	Early microbiologic outcome	Late clinical outcome	Late microbiologic outcome
1	22	KT	Ciprofloxacin (9), Meropenem (10)	Ciprofloxacin (5)	Reinfection	5	Cure	Cure	Cure	Cure
2	56	None	Ciprofloxacin (7)	Ciprofloxacin (7)	Unresolved	5	Cure	N/A	Failure	Failure
3	26	None	Ciprofloxacin (10)	Ciprofloxacin (4)	Reinfection	6	Cure	Cure	Cure	Cure
4	44	None	None	Levofloxacin (5)	Unresolved	13	Cure	Cure	Cure	Cure
5	54	None	None	Levofloxacin (14)	Unresolved	14	Cure	Cure	N/A	N/A
6	22	KT	Ciprofloxacin (14), Cefotaxim (4), Meropenem (10), Imipenem (6)	None	Relapsing	5	Cure	Cure	Cure	Cure
7	60	None	None	Ciprofloxacin (5)	Unresolved	6	Cure	Cure	N/A	N/A
8	59	DM	Ciprofloxacin (14)	Ciprofloxacin (5)	Reinfection	7	Cure	Cure	Cure	Cure
9	23	Congenital single kidney, pyeloplasty	Ciprofloxacin (4), Flumoxef (2), Cefcapene (15)	Cefcapene (4)	Unresolved	13	Failure	Failure	Cure	Cure
10	49	KT	Amikacin (20), Amoxicillin/clavulanate (7), Cefdinir (8)	Ciprofloxacin (9)	Reinfection	7	Cure	Cure	Failure	Failure
11	40	None	Ciprofloxacin (12), Cefcapen (11), Levofloxacin (18)	None	Relapsing	12	Cure	Cure	Failure	Failure
12	21	None	Ciprofloxacin (22), Meropenem (13), TMP/SMX (27)	Ciprofloxacin (3)	Unresolved	5	Cure	Cure	N/A	N/A
13	57	None	Ciprofloxacin (14), Levofloxacin (14), Amoxicillin/clavulanate (7)	Cefcapene (14)	Reinfection	7	Cure	Cure	Cure	Cure
14	53	Urethral caruncle Op	Ceftizoxime (3), Cefixime (8)	Ciprofloxacin (8)	Unresolved	5	Failure	Failure	Cure	Cure
15	45	Sling Op	Ciprofloxacin (6)	Cefixime (14)	Reinfection	7	Cure	Cure	Cure	Cure
16	51	KT	Imipene (12), Cefotaxim (19), Ciprofloxacin (17). Levofloxacin (15), Piperacillin/tazobactam (5)	None	Relapsing	16	Cure	Cure	Failure	Failure
17	27	None	Ciprofloxaci (9), Cefcapene (10)	Cefcapene (5)	Unresolved	10	Cure	Cure	Cure	Cure
18	52	Sling Op	Ceftriaxon (5), Ciprofloxacin (19), Levofloxacin (22)	Cefdinir (12)	Unresolved	11	Cure	N/A	Failure	Failure
19	58	None	Ciprofloxacin (5)	Cefcapene (13)	Unresolved	4	Cure	Cure	Cure	Cure
20	52	DM	Amikacin (22), Amoxicillin/clavulanate (13), Imipenem (15)	Fosfomycin (7)	Unresolved	8	Cure	Cure	Cure	Cure
21	41	None	Ceftriaxon (7), Levofloxacin (12)	Ciprofloxacin(6)	Unresolved	7	Cure	Cure	Cure	Cure
22	76	DM	Ciprofloxacin (13)	None	Relapsing	7	Cure	Cure	N/A	N/A
23	72	DM, Foley catheter	Ciprofloxacin (4), Ceftriaxon (8)	None	Relapsing	14	Cure	Cure	N/A	N/A
24	71	DM, Parkinson disease	None	Ciprofloxacin (6)	Unresolved	10	Cure	Cure	N/A	N/A

ESBL, extended-spectrum β-lactamases; KT, kidney transplantation recipient; DM, diabetes mellitus; TMP/SMX, trimethoprim/sulfamethoxazole; Op, operation; N/A, not assessed.

losporin (n=16, 66.7%), levofloxacin (n=7, 29.2%), carbapenem (n=6, 25%), amoxicillin/clavulanate (n=3, 12.5%), amikacin (n=2, 8.3%) and trimethoprim/sulfamethoxazole, piperacillin/tazobactam, and fosfomycin (n=1, 4.2%).

The mean treatment duration of all patients was 8.5 days. The early clinical and microbiological cure rates at 0 to 7 days after the end of the treatment were 91.7% (22/24) and 90.9% (20/22), respectively. Of the 2 clinically failed patients, progression to pyelonephritis occurred in one patient (no. 14) during treatment and she was admitted to a hospital. The other patient (no. 9) was proved to have an inflammatory mass near the urethral orifice and was completely cured after excision of the mass. The late clinical and microbiological cure rates 4 to 6 weeks after the end of treatment were 72.2% (13/18) in both. The five failed patients (27.8%) reported symptomatic recurrence and also had culture-proven bacteriuria, specifically, relapse with ESBL-producing *E. coli* in four (22.2%) and reinfection with *Klebsiella pneumoniae* in one (5.5%).

Causes of recurrent cystitis in this study could be divided into three categories. These were relapsing infection (symptomatic recurrent UTIs with the same organism following adequate therapy), reinfection (recurrent UTIs with previously isolated bacteria after treatment and with a negative intervening urine culture, or a recurrent UTI caused by a second bacterial isolate), and unresolved infection (the first proven ESBL-producing bacteriuria not responding to initial empirical antibiotic treatment). Of the 24 patients with recurrent cystitis, unresolved bacteriuria was most frequently observed in 13 (54.2%), followed by reinfection in 6 (25%) and relapse in 5 (20.8%). The group with relapsing infection seemed to have a longer treatment duration, more complicating factors, a lower late clinical cure rate, and a higher rate of late bacteriologic recurrence (Table 3).

Regarding adverse events, only two patients had mild transient nausea, which did not require discontinuation of therapy. No serious adverse events were reported in this study.

DISCUSSION

UTI is a widely prevalent infective disease globally, and more than 70% of cases are caused by *E. coli* [2]. Recently, the increase in ESBL-producing *E. coli* has become a global concern [9-11]. In the 2010 report of the Korean Antimicrobial Resistance Monitoring System, the incidence of ESBL-producing *E. coli* was 9.5% (116/1226) in community-acquired infections and 25% (9/36) in hospital-acquired infections [12]. In another report of the Korean Association of Urogenital Tract Infection and Inflammation, the prevalence of ESBL-producing *E. coli* that were isolated from female patients with uncomplicated cystitis was stated as 11.8% [13].

The recent Korean clinical guidelines for UTI recommend fluoroquinolone, β-lactam antibiotics, fosfomycin, and nitrofurantoin (NFT) for the empirical treatment of uncomplicated cystitis [14]. However, in the ESBL-producing state, third-generation cephalosporins are presumed clinically ineffective, regardless of the antimicrobial susceptibility results. Also, the plasmids encoding ESBLs carry gene-encoding resistance to other classes of antibiotics [15,16]. Therefore, the treatment options for ESBL-producing organisms are extremely limited, and it is almost impossible to choose suitable oral antibiotics. This study demonstrated that only one ESBL-producing strain (1/22, 4.5%) was susceptible to fluoroquinolones. Interestingly, susceptibility to amoxicillin/clavulanate was 63.6%, which was highest among other oral agents in this study. It appears that studies on the effectiveness of amoxicillin/clavulanate in ESBL-associated infection are needed in the near future.

There have been limited studies of available oral antibiotics for ESBL-producing *E. coli* infection. In a systemic review of fosfomycin, the antimicrobial susceptibility of fosfomycin in 1657 *E. coli* isolates that produced ESBL was shown to be 96.8% (1,604/1,657) [17]. In two studies that evaluated oral treatment with fosfomycin–trometamol of lower-level UTIs with ESBL-producing *E. coli*, the cumulative clinical cure rate of fosfomycin treatment was 93.8% (75 of 80 patients) [9,18]. However, one of these studies had a lower rate of microbiological success (41 of 52, 78.8%) [18]. Furthermore, as far as we know, antimicrobial susceptibility testing of fosfomycin in gram-negative bacteria is unavailable in Korea, because the standard susceptibility cards that are used in most Korean hospitals and institutes do not contain fosfomycin. With regard to the effect of NFT on ESBL-producing *E. coli* related to lower-level UTI, a study published in 2012 showed that all isolates were susceptible to NFT and the overall clinical and microbiological success rates were 69% (52/75) and 68% (51/75) [19]. However, in Korea, oral NFT is not produced and its sus-

TABLE 3. Patient characteristics according to subdivision of causes of recurrence

Subdivision of causes of recurrence	No.	Mean treatment duration (d)	Presence of complicating factor (%)	Early clinical cure rate	Early microbiologic cure rate	Late clinical cure rate	Late microbiologic cure rate
Unresolved	13	8.5	5/13 (38.4)	11/13 (84.6)	9/11 (81.8)	7/9 (77.7)	7/9 (77.7)
Relapsing	5	10.8	4/5 (80.0)	5/5 (100)	5/5 (100)	1/3 (33.3)	1/3 (33.3)
Reinfection	6	6.5	4/6 (66.7)	6/6 (100)	6/6 (100)	5/6 (83.3)	5/6 (83.3)

Values are presented as number (%).

ceptibility testing is unavailable. Therefore, efforts to find suitable oral antibiotics for the treatment of ESBL-producing bacterial infections are required in Korea.

There is no doubt that the treatment of choice for critical infections caused by ESBL-producing gram-negative bacteria is parenteral carbapenem [8,20]. However, in the case of simple cystitis without systemic symptoms, for which treatments fail due to ESBL-producing *E. coli*, the use of carbapenem such as imipenem or meropenem could pose a dilemma, because the three to four times daily parenteral treatments require hospitalization, which results in increased cost and time.

Ertapenem is a parenteral and long-acting carbapenem. It is more highly protein-bound and has a longer half-life than does imipenem or meropenem. Its longer half-life and once-daily parenteral dosage of 1 g make it an ideal choice for outpatient parenteral antibiotic therapy [21]. It has been shown to have good in vitro activity against ESBL-producing *Enterobacteriaceae*. However, ertapenem has limited activity against isolates of nonfermentative gram-negative bacilli such as *Pseudomonas aeruginosa* and *Acinetobacter* spp. and is the least active carbapenem against enterococci [22]. Ertapenem should not be used empirically to treat patients with nosocomial infection because *Pseudomonas aeruginosa* and other nonfermentative gram-negative bacilli are likely pathogens in this setting.

Despite the few observational data regarding clinical outcomes with ertapenem, recent studies reported the clinical efficacy of ertapenem in the treatment of ESBL-producing infections [23-25]. In this study, all 24 ESBL strains were found to be susceptible to carbapenem. Overall, its early clinical and bacterial efficacies were 91.7% (22/24) and 90.9% (20/22), respectively. The results were comparable to the following expected clinical and microbiological efficacies of common oral agents for acute uncomplicated cystitis, which were described in the 2010 update of the guidelines for the treatment of acute uncomplicated UTIs in women by the Infectious Diseases Society of America: NFT (100 mg twice daily for 5–7 days, 93% and 88%), fluoroquinolones (the dose varies by agent, 3-day regimen, 90% and 91%), and trimethoprim/sulfamethoxazole (160/800 mg twice daily for 3 days, 93% and 94%), respectively [26]. However, the late clinical and bacterial efficacies dropped to 72.2%, which was especially predominant in relapsing infection (33.3%). Physicians should understand this fact before treatment and future studies should focus on the management of relapsing infection due to bacterial persistence.

The main limitation of this study was the fact that it was a retrospective study with a relatively small number of cases but was not a randomized or controlled study. Different treatment duration and irregular follow-up may disturb exact interpretation. In addition, because this was a retrospective study, we did not have control cultures for all cases.

The results of this study suggest that patients with recurrent cystitis caused by ESBL-producing *E. coli*, with no suitable oral antibiotic therapy, can be treated effectively as outpatients with once-daily parenteral ertapenem.

CONCLUSIONS

The emergence of and gradual increase in multidrug-resistant ESBL-producing *E. coli* have become global threats to human health. The choice of suitable oral antibiotics is extremely limited in the ESBL-producing state. Finding regionally useful oral antibiotics that are effective against UTIs caused by ESBL-producing *E. coli* should be of high priority. The administration of once-daily parenteral ertapenem to outpatients may be a useful secondary therapeutic option for recurrent cystitis caused by ESBL-producing *E. coli* in patients in whom empirical oral antibiotic treatment has failed.

CONFLICTS OF INTEREST

The authors have nothing to disclose.

ACKNOWLEDGMENTS

This study was supported by a research fund from Chosun University, 2013.

REFERENCES

1. Ronald AR, Nicolle LE, Stamm E, Krieger J, Warren J, Schaeffer A, et al. Urinary tract infection in adults: research priorities and strategies. Int J Antimicrob Agents 2001;17:343-8.
2. Valiquette L. Urinary tract infections in women. Can J Urol 2001;8 Suppl 1:6-12.
3. Warren JW, Abrutyn E, Hebel JR, Johnson JR, Schaeffer AJ, Stamm WE. Guidelines for antimicrobial treatment of uncomplicated acute bacterial cystitis and acute pyelonephritis in women. Infectious Diseases Society of America (IDSA). Clin Infect Dis 1999;29:745-58.
4. Hawser SP, Bouchillon SK, Hoban DJ, Badal RE. In vitro susceptibilities of aerobic and facultative anaerobic Gram-negative bacilli from patients with intra-abdominal infections worldwide from 2005-2007: results from the SMART study. Int J Antimicrob Agents 2009;34:585-8.
5. Chung A, Arianayagam M, Rashid P. Bacterial cystitis in women. Aust Fam Physician 2010;39:295-8.
6. Mohsin R, Siddiqui KM. Recurrent urinary tract infections in females. J Pak Med Assoc 2010;60:55-9.
7. Pitout JD, Laupland KB. Extended-spectrum beta-lactamase-producing Enterobacteriaceae: an emerging public-health concern. Lancet Infect Dis 2008;8:159-66.
8. Shah PM. Parenteral carbapenems. Clin Microbiol Infect 2008;14 Suppl 1:175-80.
9. Rodriguez-Bano J, Alcala JC, Cisneros JM, Grill F, Oliver A, Horcajada JP, et al. Community infections caused by extended-spectrum beta-lactamase-producing Escherichia coli. Arch Intern Med 2008;168:1897-902.
10. Pitout JD, Nordmann P, Laupland KB, Poirel L. Emergence of Enterobacteriaceae producing extended-spectrum beta-lactamases (ESBLs) in the community. J Antimicrob Chemother 2005;56:52-9.

11. Rodriguez-Bano J, Paterson DL. A change in the epidemiology of infections due to extended-spectrum beta-lactamase-producing organisms. Clin Infect Dis 2006;42:935-7.
12. Lee SJ, Lee DS, Choe HS, Shim BS, Kim CS, Kim ME, et al. Antimicrobial resistance in community-acquired urinary tract infections: results from the Korean Antimicrobial Resistance Monitoring System. J Infect Chemother 2011;17:440-6.
13. Kim ME, Ha US, Cho YH. Prevalence of antimicrobial resistance among uropathogens causing acute uncomplicated cystitis in female outpatients in South Korea: a multicentre study in 2006. Int J Antimicrob Agents 2008;31 Suppl 1:S15-8.
14. The Korean Society of Infectious Diseases, The Korean Society for Chemotherapy, Korean Association of Urogenital Tract Infection and Inflammation, The Korean Society of Clinical Microbiology. Clinical guideline for the diagnosis and treatment of urinary tract infections: asymptomatic bacteriuria, uncomplicated & complicated urinary tract infections, bacterial prostatitis. Infect Chemother 2011;43:1-25.
15. Yang K, Guglielmo BJ. Diagnosis and treatment of extended-spectrum and AmpC beta-lactamase-producing organisms. Ann Pharmacother 2007;41:1427-35.
16. Yu Y, Zhou W, Chen Y, Ding Y, Ma Y. Epidemiological and antibiotic resistant study on extended-spectrum beta-lactamase-producing Escherichia coli and Klebsiella pneumoniae in Zhejiang Province. Chin Med J (Engl) 2002;115:1479-82.
17. Falagas ME, Kastoris AC, Kapaskelis AM, Karageorgopoulos DE. Fosfomycin for the treatment of multidrug-resistant, including extended-spectrum beta-lactamase producing, Enterobacteriaceae infections: a systematic review. Lancet Infect Dis 2010; 10:43-50.
18. Pullukcu H, Tasbakan M, Sipahi OR, Yamazhan T, Aydemir S, Ulusoy S. Fosfomycin in the treatment of extended spectrum beta-lactamase-producing Escherichia coli-related lower urinary tract infections. Int J Antimicrob Agents 2007;29:62-5.
19. Tasbakan MI, Pullukcu H, Sipahi OR, Yamazhan T, Ulusoy S. Nitrofurantoin in the treatment of extended-spectrum β-lactamase-producing Escherichia coli-related lower urinary tract infection. Int J Antimicrob Agents 2012;40:554-6.
20. Ramphal R, Ambrose PG. Extended-spectrum beta-lactamases and clinical outcomes: current data. Clin Infect Dis 2006;42 Suppl 4:S164-72.
21. Bazaz R, Chapman AL, Winstanley TG. Ertapenem administered as outpatient parenteral antibiotic therapy for urinary tract infections caused by extended-spectrum-beta-lactamase-producing Gram-negative organisms. J Antimicrob Chemother 2010;65: 1510-3.
22. Jacoby G, Han P, Tran J. Comparative in vitro activities of carbapenem L-749,345 and other antimicrobials against multiresistant gram-negative clinical pathogens. Antimicrob Agents Chemother 1997;41:1830-1.
23. Berg ML, Crank CW, Philbrick AH, Hayden MK. Efficacy of ertapenem for consolidation therapy of extended-spectrum beta-lactamase-producing gram-negative infections: a case series report. Ann Pharmacother 2008;42:207-12.
24. Lye DC, Wijaya L, Chan J, Teng CP, Leo YS. Ertapenem for treatment of extended-spectrum beta-lactamase-producing and multidrug-resistant gram-negative bacteraemia. Ann Acad Med Singapore 2008;37:831-4.
25. Lee NY, Huang WH, Tsui KC, Hsueh PR, Ko WC. Carbapenem therapy for bacteremia due to extended-spectrum β-lactamase-producing Escherichia coli or Klebsiella pneumoniae. Diagn Microbiol Infect Dis 2011;70:150-3.
26. Gupta K, Hooton TM, Naber KG, Wullt B, Colgan R, Miller LG, et al. International clinical practice guidelines for the treatment of acute uncomplicated cystitis and pyelonephritis in women: A 2010 update by the Infectious Diseases Society of America and the European Society for Microbiology and Infectious Diseases. Clin Infect Dis 2011;52:e103-20.