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ORIGINAL ARTICLE

Comparison of the effectiveness and antibiotic cost among ceftriaxone, ertapenem, and levofloxacin in treatment of community-acquired complicated urinary tract infections

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Purpose: To study characteristics of patients with community-acquired complicated urinary tract infections (cUTIs) and to compare effectiveness and antibiotic cost of treatment with ceftriaxone (CRO), levofloxacin (LVX), and ertapenem (ETP).
Methods: This retrospective study enrolled patients who had community-acquired cUTIs admitted to Division of Infectious Diseases in a single medical center from January 2011 to March 2013. Effectiveness, antibiotic cost, and clinical characteristics were compared among patients treated with CRO, LVX, and ETP.
Results: There were 358 eligible cases, including 139 who received CRO, 128 treated with ETP, and 91 with LVX. The most common pathogen was *Escherichia coli*. The susceptibilities of these three agents were higher and more superior than first-line antibiotics. Treatment with ETP was associated with a significantly shorter time to defervescence since admission (CRO: 39 hours, ETP: 30 hours, and LVX: 38 h; $p = 0.031$) and shorter hospitalization stay (CRO: 4 days, ETP: 3

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days, and LVX: 4 days; $p < 0.001$). However, the average antibiotic costs in the CRO group were significantly lower than that in the other two groups [CRO: 62.4 United States dollars (USD), ETP: 185.33 USD, and LVX: 204.85 USD; $p < 0.001$].
Conclusion: The resistance of cUTIs isolates to first-line antibiotic is high. Using ETP, CRO, and LVX in the treatment of cUTIs for good clinical response should be suggested. Among the three agents, ETP had better susceptibility than CRO and LVX, reached defervescence sooner, and was associated with shorter hospital stays. However, using CRO in cUTIs was less expensive than the other two agents.

Introduction

Urinary tract infections (UTIs) are responsible for approximately 7 million physician office visits and more than 1 million hospitalizations in the United States each year.[1–3] Most of these cases are uncomplicated infections of the bladder in otherwise healthy young women that are easily managed with short-term antimicrobial therapy. However, complicated UTIs (cUTIs) may occur in both sexes and all age groups and are frequently associated with either anatomical or functional urinary tract abnormalities.[4,5] Treatment of cUTIs is generally less successful because of the emergence of antimicrobial resistant strains, and such cases are a significant challenge for clinicians.[1,6] Ceftriaxone (CRO), ertapenem (ETP), and levofloxacin (LVX) are recommended in the treatment guidelines for cUTIs.[4,7,8] Research has compared treatment of cUTIs with CRO and ETP, with CRO and LVX, but no study has compared the treatment outcome between CRO, ETP, and LVX.

This study compared treatment outcomes of CRO, ETP, and LVX and antibiotic costs related to admitted patients with cUTIs.

Methods

Patient population and clinical evaluation

This study used retrospective chart review and was approved by the Institutional Review Board of the Tri-Service General Hospital (TSGHIRB Approval Number: 097-05-28), an 1800-bed medical center in Taipei, Taiwan. All the patients enrolled were those admitted to Division of Infection Diseases (ID) with cUTIs during January 2011 to March 2013.

All patients who received a diagnosis within 48 hours of admission and in whom health care associated infections were excluded were considered to have community-acquired infections. All patients who were at least 18 years old and had cUTIs with acute pyelonephritis (APN) that required parenteral antibiotic therapy were eligible. Criteria for APN included fever, flank pain or costovertebral angle knocking or percussion tenderness, pyuria ($\geq$10 white blood cells per high-power field).[9] Criteria for cUTIs in males were symptoms/signs of UTI. Females were additionally required to have either an indwelling catheter, current bladder catheterization, instrumentation of the urinary tract, functional or anatomic abnormality of the urinary tract[9] including foreign bodies (e.g., stones, indwelling catheters or other drainage devices, obstruction), immunosuppression, renal insufficiency, and comorbid illness.[4]

Individuals with other infections since admission or during admission who received antibiotics other than the three study agents, patients with changing treatment regimens during admission, those with different treatment regimens by the physician of the emergency department, patients who received surgery during admission, pregnancy or lactation in women, patients with any rapidly progressive or terminal disease, or individuals with prior to renal transplantation were excluded. Patients in whom health care-associated infections had been diagnosed were excluded if any of the following criteria were present: $>$48 hours of hospitalization within the past 90 days, receipt of hemodialysis, administration of intravenous medication or home wound care in the past 30 days, or residence in a nursing home or long-term care facility. Decision regarding the antibiotic therapy was made by the attending physicians who took care of the patients. The initial antibiotic regimen was administered after blood and urine samples had been taken for culture.

Effectiveness and cost variables

The primary outcome was the time to defervescence after admission was calculated since arrival on the ward, and the secondary outcome was duration of hospital stay. The antibiotic cost was also calculated as the sum of all antibiotic usage during hospital course.

Bacterial cultures and antimicrobial susceptibility tests

Fresh urine and blood samples were delivered to the laboratory and were processed according to standard procedures soon after UTIs were confirmed in the emergency department or ward. Blood and urine samples were plated on MacConkey and CPS3 agar and processed using an automated blood culture system (VITEK 2 complete ID/AST Automation system; bioMérieux, Mercy l'Etoile, France). Antibiotic susceptibility testing was determined using VITEK 2 complete ID/AST Automation system in accordance with

criteria of the Clinical and Laboratory Standards Institute, M100-S20[10] for the following antibiotics: ampicillin, cefazolin, gentamicin, amikacin, ampicillin-sulbactam, trimethoprim-sulfamethoxazole, piperacillin-tazobactam, ceftazidime, CRO, imipenem, LVX, cefepime, nitrofurantoin, and ETP for gram-negative bacteria (GNB). A difference of at least 5 mm between the zone diameters of either the cefotaxime or ceftazidime disks and their respective cephalosporin/clavulanate disks was considered to be phenotypic confirmation for the production of extended-spectrum β-lactamase (ESBL) according to the criteria of the Clinical and Laboratory Standards Institute, M100-S19.[11]

Statistical analysis

To assess differences, the Chi-square test with Yates correction or Fisher's exact test was used to compare the discrete variables; the Student *t* test or Mann–Whitney rank-sum test was used to analyze continuous variables. A *p* value <0.05 was considered statistically significant. All the analyses were processed with SPSS software version 18.0 (SPSS Inc., Chicago, IL, USA).

Results

Patient population and clinical evaluation

There were 639 patients admitted to the ward of infectious diseases (ID) Section under diagnosis of cUTIs from January 2011 to March 2013. A total of 358 patients met our inclusion criteria, including 139 who received CRO, 128 received ETP, and 91 received LVX (Fig. 1).

The demographic and clinical characteristics of the three groups were shown in Table 1. The most common underlying disease was hypertension in the three groups (34.1–50.0%; $p = 0.064$). The LVX group had significantly more patients with flank pain [CRO: 23.0% (32/139), ETP: 29.7% (38/128), LVX: 39.6% (36/91); $p = 0.027$]; however, the CRO group had significantly more patients with chills [CRO: 59.0% (82/139), ETP: 38.3% (49/128), LVX: 44.0% (40/91); $p = 0.002$].

Effectiveness and cost

The clinical outcomes and antibiotic costs of patients in the three groups were shown in Table 2. In the ETP group, the patients had shorter time to defervescence since admission compared to the other two groups (CRO: 39 hours, ETP: 30 hours, and LVX: 38 hours; $p = 0.031$). In the ETP group, patients also had shorter hospitalization stay (CRO: 4 days, ETP: 3 days, and LVX: 4 days; $p < 0.001$). The average antibiotic costs in CRO group was significantly lower than that in the other two groups [CRO: 62.4 United States dollars (USD), ETP: 185.33 USD, and LVX: 204.85 USD; $p < 0.001$].

Bacterial cultures and antimicrobial susceptibility tests

There were 208 GNB and 28 gram-positive cocci (GPC) and two *Candida* spp. growth in the 358 urine isolates. Bacteremia was found in 86 patients (28.0%). The most common GNB pathogens were *Escherichia coli*, *Klebsiella pneumoniae*, and *Proteus mirabilis* (Fig. 2). Among the 28 isolates of GPC, 17 were *Enterococcus* spp., six were *Streptococcus* spp., and five were *Staphylococcus* spp. The

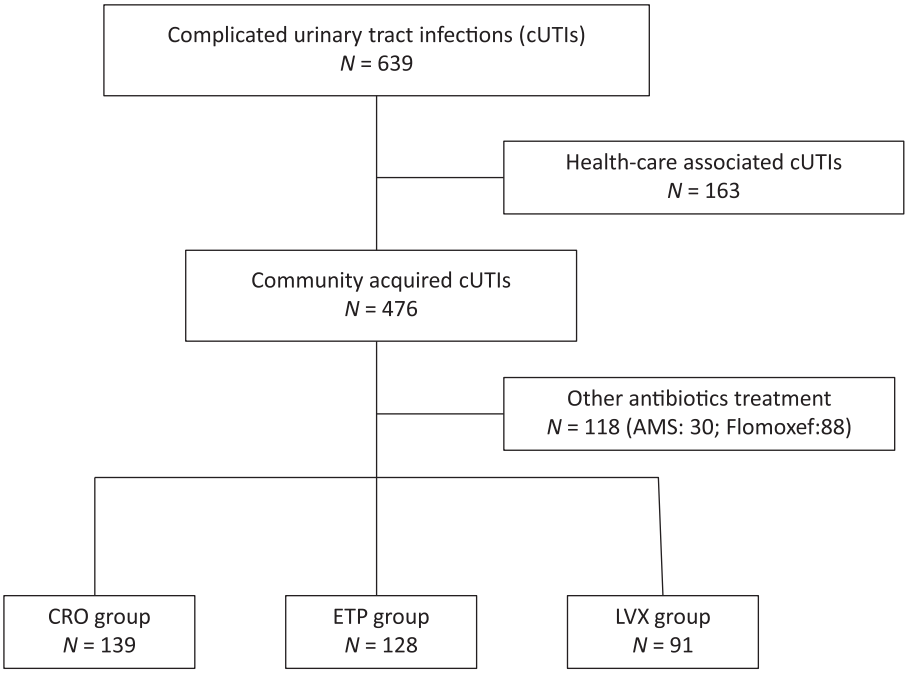

Figure 1. Flow diagram of complicated urinary tract infections of enrolled participants. AMS = ampicillin-sulbactam; CRO = ceftriaxone; cUTI = complicated urinary tract infection; ETP = ertapenem; LVX = levofloxacin.

Table 1 Demographic and clinical characteristics of patients with complicated urinary tract infections

Characteristic	Ceftriaxone group ($N = 139$)	Ertapenem group ($N = 128$)	Levofloxacin group ($N = 91$)	p
Mean ± SD/n (%)				
Mean age (y)	64.49 ± 20.14	67.17 ± 20.78	61.03 ± 16.90	0.075
Sex				0.465
Male	32 (23.0)	38 (29.7)	24 (26.4)	
Female	107 (77.0)	90 (70.3)	67 (73.6)	
Underlying disease				
Hypertension	61 (43.9)	64 (50.0)	31 (34.1)	0.064
Diabetes mellitus	34 (24.5)	31 (24.2)	25 (27.5)	0.837
Chronic liver disease	3 (2.2)	4 (3.1)	1 (1.1)	0.605
chronic renal disease	10 (7.1)	8 (6,2)	6 (6.5)	0.812
Urolithiasis[a]	12 (8.6)	9 (7.0)	7 (7.7)	0.887
Malignant disorder	13 (9.4)	10 (7.8)	10 (11.0)	0.724
Indwelling urinary catheter[b]	18 (13.0)	16 (12.5)	4 (4.4)	0.083
Clinical presentations				
Fever	121 (87.0)	109 (85.1)	78 (85.7)	0.843
Dysuria	38 (27.3)	39 (30.5)	33 (36.3)	0.356
Frequency	34 (24.5)	25 (19.5)	30 (33.0)	0.076
Flank pain	32 (23.0)	38 (29.7)	36 (39.6)	0.027
Chills	82 (59.0)	49 (38.3)	40 (44.0)	0.002
Microorganism				
ESBL-producing strains[c]	2 (1.4)	6 (4.7)	1 (1.1)	0.145

[a] Including renal stone, ureteral stone, bladder stone.
[b] Including percutaneous nephrostomy, suprapubic catheter, and Foley catheter.
[c] ESBL = extended-spectrum β-lactamase; SD = standard deviation.

antimicrobial susceptibilities of the 208 isolates GNB isolates were shown in Table 3. The most effective antibiotics were amikacin, imipenem, and ETP (98.1—100%), followed by cefepime, ceftazidime, and CRO (93.8—95.7%). The susceptibility to β-lactam agents ranged from 60.3% to 99.5% and the susceptibility to LVX was 87.0%. The susceptibility to LVX was significantly lower than ETP and CRO (87.0%, 98.1%, and 93.8%, respectively, $p < 0.001$). The first-generation cephalosporin, ampicillin, trimethoprim-sulfamethoxazole, and ampicillin-sulbactam have lower susceptibilities (0.5—60.3%). ESBL strains were few among the isolates (9/208, 4.3%). There were no statistical differences among the three groups in their antimicrobial susceptibilities.

Discussion

The study compared the clinical characteristics and antibiotic costs in patients with cUTIs receiving three different antibiotics. Compared to patients in the other two groups, ETP group had shorter time to defervescence since admission and shorter hospitalization stay. The antibiotic cost was significant lower in CRO group. *E. coli*, *K. pneumoniae*, and *P. mirabilis* still were the most frequent encountered pathogens in the current study. The antimicrobial susceptibilities were generally good in the three agents, but poor in cefazolin, ampicillin, trimethoprim-sulfamethoxazole, and ampicillin-sulbactam.

Table 2 Clinical outcomes and antibiotic cost of patients with complicated urinary tract infections

	Ceftriaxone group ($N = 139$)	Ertapenem group ($N = 128$)	Levofloxacin group ($N = 91$)	p
Median (Q1—Q3)/n (%)				
Time to defervescence since admission (h)[a]	39 (19—74)	30 (4.5—59.5)	38 (9—64)	0.03
Hospital day (day)	4 (4—6)	3 (3—5)	4 (3—6)	<0.01
Antibiotic cost (USD)	62.4 (62.4—78)	185.33 (139—231.67)	204.85 (204.85—256.06)	<0.01
Mortality during admission	0 (0.0)	0 (0.0)	0 (0.0)	—

[a] Time to defervescence since admission was calculated since arrived to ward.
USD = United States dollars.

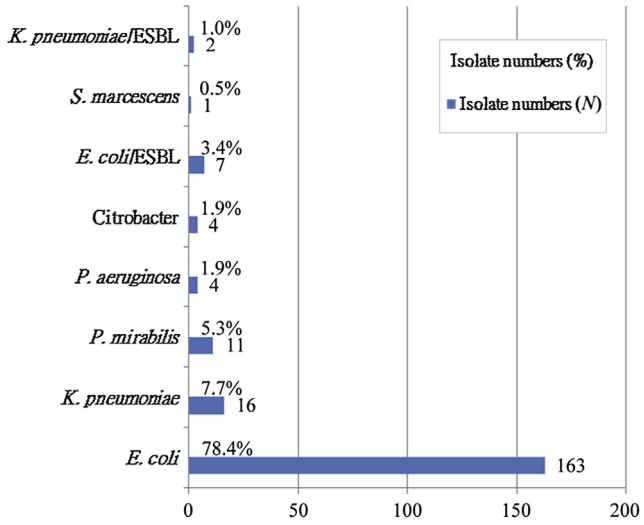

Figure 2. Bacterial species and isolate numbers of 208 isolates causing complicated urinary tract infections.

GNB were generally the most frequently isolated pathogen in cUTIs, especially *E. coli*, *K. pneumoniae*, and *P. mirabilis*. Compared to our previous study 10 years ago,[12] the isolates in the current study showed lower susceptibility to first-line antibiotics. This result suggested that for the increasing antimicrobial resistances in community-acquired cUTIs, empirical antimicrobial treatment should be carefully decided.

Our results showed that ETP was more effective than CRO or LVX in defervescence and having shorter hospitalization. It has previous been described that ETP was more active against the enteric gram-negative pathogens than ceftriaxone and piperacillin–tazobactam.[13] Even though there was no statistical difference in antimicrobial susceptibilities among the three drugs, the isolates had higher susceptibility to ETP. This may also explain why patients in the ETP group had a better response. In addition, CRO and ETP have excellent pharmacokinetics presenting higher blood and urine concentrations above minimum inhibitory concentrations than LVX.[14–17] Another important issue was the generic formulations of CRO. During the study period, there were many generic formulations of CRO available in Taiwan (and in our hospital). The generic CROs accounted for more than half of the clinical prescriptions of all CROs in our hospital.[18] It might also play a role in the clinical outcomes.

There is an increase of fluoroquinolone resistance in GNBs worldwide.[19,20] Bouchillon et al[21] reported that fluoroquinolone resistance rates varied widely among different countries (6–75%). The isolates from our study had an average LVX susceptibility rate of 87.0%. Lu et al[22] reported that the percentage of ESBL-producers was 28.2% among all UTI pathogens in the Asia-Pacific region, and in Taiwan they were 15% and 27% in *E. coli* and *K. pneumoniae* isolates. In contrast to CRO and LVX, ETP showed excellent activity against ESBL-producing strains and even those are resistant to β-lactam/β-lactamase inhibitor combination agents.[23–25]

This study is subject to several limitations regularly found in retrospective studies. Several confounding factors could not be well controlled in the three groups, such as the decisions of antibiotic selection cannot be well controlled among patients, and the styles of patient care were also varied among different doctors. However, our sample size was relatively big and the patient characteristics between groups were similar. A well-conducted prospective study may be necessary in the future to elucidate the differences in treating cUTIs among the three agents.

In conclusion, the resistance of cUTIs isolates to first-line antibiotics is high. ETP, CRO, and LVX in the treatment of cUTIs had good clinical response. Among the three agents, ETP had better susceptibility than CRO and LVX, reached defervescence sooner, and was associated with shorter

Table 3 The antimicrobial susceptibilities of 208 gram-negative isolates causing complicated urinary tract infections

	Ceftriaxone group (91/139; 65.4%)	Ertapenem group (73/128; 57%)	Levofloxacin group (44/91; 48.3%)	Total (N = 208)	p
N (%)					
AM	30 (33.7)	16 (22.5)	17 (38.6)	63 (30.9)	0.236
CZ	0 (0.0)	1 (1.4)	0 (0.0)	1 (0.5)	0.600
GM	80 (87.9)	62 (84.9)	40 (90.9)	182 (87.5)	0.654
AN	91 (100.0)	73 (100.0)	44 (100.0)	208 (100.0)	–
AMS	54 (60.7)	39 (54.9)	30 (68.2)	123 (60.3)	0.545
SXT	53 (59.6)	36 (50.7)	21 (47.7)	110 (53.9)	0.348
TZP	84 (92.3)	68 (93.2)	42 (95.5)	194 (93.3)	0.916
CAZ	87 (95.6)	67 (91.8)	43 (97.7)	197 (94.7)	0.157
CRO	87 (95.6)	65 (89.0)	43 (97.7)	195 (93.8)	0.106
IPM	91 (100.0)	72 (98.6)	44 (100.0)	207 (99.5)	0.395
LVX	82 (90.1)	58 (79.5)	41 (93.2)	181 (87.0)	0.144
FEP	89 (97.8)	67 (91.8)	43 (97.7)	199 (95.7)	0.128
F/M	77 (86.5)	60 (84.5)	38 (86.4)	175 (85.8)	0.326
ETP	89 (97.8)	71 (97.3)	44 (100.0)	204 (98.1)	–

AM = ampicillin; AMS = ampicillin-sulbactam; AN = amikacin; CAZ = ceftazidime; CRO = ceftriaxone; CZ = cefazolin; ETP = ertapenem; F/M = nitrofurantoin; GM = gentamycin; IPM = imipenem; LVX = levofloxacin; SXT = trimethoprim-sulfamethoxazole; TZP = piperacillin-tazobactam.

hospital stays. However, using CRO in cUTIs was less expensive than the other two agents.

Conflict of interest

None.

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References

1. Stamm WE, Hooton TM. Management of urinary tract infections in adults. *N Engl J Med* 1993;**329**:1328—34.
2. Wu YH, Chen PL, Hung YP, Ko WC. Risk factors and clinical impact of levofloxacin or cefazolin nonsusceptibility or ESBL production among uropathogens in adults with community-onset urinary tract infections. *J Microbiol Immunol Infect* 2014;**47**:197—203.
3. Yang YS, Ku CH, Lin JC, Shang ST, Chiu CH, Yeh KM, et al. Impact of Extended-spectrum b-lactamase-producing *Escherichia coli* and *Klebsiella pneumoniae* on the outcome of community-onset bacteremic urinary tract infections. *J Microbiol Immunol Infect* 2010;**43**:194—9.
4. Mazzulli T. Diagnosis and management of simple and complicated urinary tract infections (UTIs). *Can J Urol* 2012;**19**:42—8.
5. Pallett A, Hand K. Complicated urinary tract infections: practical solutions for the treatment of multiresistant Gram-negative bacteria. *J Antimicrob Chemother* 2010;**65**:iii25—33.
6. 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. *Clin Infect Dis* 1999;**29**:745—58.
7. 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.
8. Infectious Disease Society of the Republic of China; Medical Foundation in Memory of Dr. Deh-Lin Cheng; Foundation of Professor Wei-Chuan Hsieh for Infectious Diseases Research and Education; Lee CY's Research Foundation for Pediatric Infectious Diseases and Vaccine. Guidelines for antimicrobial therapy of urinary tract infections in Taiwan. *J Microbiol Immunol Infect* 2000;**33**:271—2.
9. Center for Drug Evaluation and Research. Guidance for industry. Complicated urinary tract infections and pyelonephritis-developing antimicrobial drugs for treatment. Available at, http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm070981.pdf [accessed February 2012].
10. CLSI—Clinical Laboratory Standards Institute. *Performance standards for antimicrobial susceptibility testing: M100—S20*. Wayne, PA: Clinical Laboratory Standards Institute; 2010.
11. CLSI—Clinical Laboratory Standards Institute. *Performance standards for antimicrobial susceptibility testing: M100—S19*. Wayne, PA: Clinical Laboratory Standards Institute; 2009.
12. Lau SM, Peng MY, Chang FY. Resistance rates to commonly used antimicrobials among pathogens of both bacteremic and non-bacteremic community-acquired urinary tract infection. *J Microbiol Immunol Infect* 2004;**37**:185—91.
13. Gesser RM, McCarroll K, Teppler H, Woods GL. Effectiveness of ertapenem in the treatment of serious infections caused by Enterobacteriaceae: analysis of pooled clinical trial data. *J Antimicrob Chemother* 2003;**51**:1253—60.
14. Nix DE, Majumdar AK, DiNubile MJ. Pharmacokinetics and pharmacodynamics of ertapenem: an overview for clinicians. *J Antimicrob Chemother* 2004;**53**:ii23—8.
15. Perry TR, Schentag JJ. Clinical use of ceftriaxone a pharmacokinetic-pharmacodynamic perspective on the impact of minimum inhibitory concentration and serum protein binding. *Clin Pharmacokinet* 2001;**40**:685—94.
16. Deguchi T, Nakane K, Yasuda M, Shimizu T, Monden K, Arakawa S, et al. Microbiological outcome of complicated urinary tract infections treated with levofloxacin: a pharmacokinetic/pharmacodynamic analysis. *Int J Antimicrob Agents* 2010;**35**:573—7.
17. Nicolle L, Duckworth H, Sitar D, Bryski L, Harding G, Zhanel G. Pharmacokinetics/pharmacodynamics of levofloxacin 750 mg once daily in young women with acute uncomplicated pyelonephritis. *Int J Antimicrob Agents* 2008;**31**:287—9.
18. Schito GC, Keenan MH. Predicting the clinical effectiveness of generic formulations of ceftriaxone. *J Chemother* 2005;**17**:33—40.
19. Aypak C, Altunsoy A, Duzgun N. Empiric antibiotic therapy in acute uncomplicated urinary tract infections and fluoroquinolone resistance: a prospective observational study. *Ann Clin Microbiol Antimicrob* 2009;**8**:27.
20. Shigemura K, Arakawa S, Miura T, Nakano Y, Tanaka K, Fujisawa M. Significance of fluoroquinolone-resistant *Escherichia coli* in urinary tract infections. *Jpn J Infect Dis* 2008;**61**:226—8.
21. Bouchillon S, Hoban DJ, Badal R, Hawser S. Fluoroquinolone resistance among gram-negative urinary tract pathogens: global smart program result, 2009-2020. *Open Mircobiol J* 2012;**6**:74—8.
22. Lu PL, Liu YC, Toh HS, Lee YL, Liu YM, Ho CM, et al. Epidemiology and antimicrobial susceptibility profiles of Gram-negative bacteria causing urinary tract infections in the Asia-Pacific region: 2009—2010 results from the Study for Monitoring Antimicrobial Resistance Trends (SMART). *Int J Antimicrob Agents* 2012;**40**:37—43.
23. Livermore DM, Carter MW, Baqel S, Wiedemann B, Baquero F, Loza E, et al. In vitro activities of ertapenem (MK-0826) against recent clinical bacteria collected in Europe and Australia. *Antimicrob Agents Chemother* 2001;**45**:1860—7.
24. Fuchs PC, Barry AL, Brown SD. In vitro activities of ertapenem (MK-0826) against clinical bacterial isolates from 11 North American medical centers. *Antimicrob Agents Chemother* 2001;**45**:1915—8.
25. Livermore DM, Oakton KJ, Carter MW, Warner M. Activity of ertapenem (MK-0826) versus Enterobacteriaceae with potent β-lactamases. *Antimicrob Agents Chemother* 2001;**45**:2831—7.