Swiss Medical Weekly
Formerly: Schweizerische Medizinische Wochenschrift
The European Journal of Medical Sciences

Original article | Published 15 July 2010, doi:10.4414/smw.2010.13059
Cite this as: Swiss Med Wkly. 2010;140:w13059

Risk factors for urinary tract infections due to ciprofloxacin-resistant *Escherichia coli* in a tertiary care urology department in Switzerland

Joëlle Nicoletti[a], Stefan P. Kuster[a]*, Tullio Sulser[b], Reinhard Zbinden[c], Christian Ruef[a], Bruno Ledergerber[a], Rainer Weber[a]*

[a] Division of Infectious Diseases and Hospital Epidemiology, University Hospital Zurich, University of Zurich, Zurich, Switzerland
[b] Department of Urology, University Hospital Zurich, Zurich, Switzerland
[c] Institute of Medical Microbiology, University of Zurich, Zurich, Switzerland

* Contributed equally.

Correspondence:
Prof. Dr. med. Rainer Weber
Division of Infectious Diseases and Hospital Epidemiology
University Hospital Zurich
University of Zurich
Raemistrasse 100
CH-8091 Zurich
Switzerland
E-Mail: rainer.weber@usz.ch

Summary

Questions under study: Monitoring of antimicrobial resistance is a key component of antibiotic stewardship programs. In 2007, a significantly higher resistance rate of *Escherichia coli* to ciprofloxacin was found at the Department of Urology, University Hospital Zurich, Switzerland, when compared to other hospital units. Thus, we aimed to determine the risk factors for this increased fluoroquinolone resistance in outpatients and inpatients with urinary tract infection (UTI) or colonisation with *E. coli*.

Methods: We performed a cross sectional study including 275 patients of the Department of Urology in whom *E. coli* was isolated from urine or blood cultures between 01.01.2006 and 31.08.2007. Clinical data were collected from patients' records using a structured questionnaire. Multivariable analysis was performed for the detection of risk factors.

Results: Ciprofloxacin-resistant *E. coli* was detected in 22% of patients. Risk factors for ciprofloxacin-resistant *E. coli* included prior use of fluoroquinolones (odds ratio [OR] (95% confidence intervals): 2.24 (1.08–4.62), p = 0.030), prior urinary tract catheterisation (OR: 2.41 (1.02–5.67), p = 0.044) and recurrent UTIs (OR: 2.26 (1.07–4.78), p = 0.032). 60.8% of all prescriptions in urinary tract infections were for fluoroquinolones, and this antibiotic class was the empiric antibiotic regimen of choice in 72.5% of all acute, uncomplicated, urinary tract infections.

Conclusions: The increasing prevalence of ciprofloxacin-resistant *E. coli* makes empiric therapy in UTIs with this agent questionable, especially in patients with one or several of the above mentioned risk factors. Due to the increasing resistance rate, continuous surveillance and susceptibility testing in individual patients, particularly with complicated UTIs, is indispensable for adequate therapy.

Key words: *Escherichia coli; ciprofloxacin; fluoroquinolones; antibacterial drug resistance; urinary tract infections; urology*

Introduction

Urinary tract infections (UTIs) are common infections among inpatients and outpatients, ranking second only to respiratory infections, and thus, are a frequent cause for prescription of antibiotics [1]. Common pathogens causing uncomplicated UTIs are *Escherichia coli* (75–90% of UTIs) and *Staphylococcus saprophyticus* (5–15% of UTIs, particularly in younger women). Occasionally, *Proteus mirabilis*, *Klebsiella* spp. or enterococci are isolated from urine samples [2]. Fluoroquinolones are often prescribed empirically and as a first choice in patients with UTIs, achieving high concentrations in urine and showing a broad antibacterial spectrum. In 2000, fluoroquinolones were prescribed for treatment of acute, uncomplicated UTIs in Switzerland in 64% of cases [3]. Knowledge of the most frequent microorganisms and their susceptibility pattern are the basis for empirical antimicrobial therapy, especially in UTIs, as susceptibility testing is often not performed in the community setting. Unfortunately, this diagnostic and therapeutic approach is becoming more and more limited because of increasing resistance to commonly used antimicrobial drugs.

Across Europe, levels of antibiotic consumption show great variations [4], with the use of fluoroquinolones being

highest in Portugal and Spain. As the emergence of resistance is associated with high antibiotic consumption [5, 6], it is not surprising that resistance to ciprofloxacin in *E. coli* shows great geographical variations, too, reaching high levels in southern Europe and low levels in northern European countries [6–8]. In addition to attentive monitoring of resistance patterns, the identification of risk factors for infections with resistant strains may contribute to improved empirical treatment. Factors associated with resistance to ciprofloxacin in *E. coli* reported in previous studies are urinary tract abnormalities, older age, previous antimicrobial therapy (especially quionolone therapy), urinary catheterisation, recurrent UTIs, male gender and presence of complicated UTI [9–13]. In our hospital, resistance rates of *E. coli* to ciprofloxacin in inpatients range from as low as 4.9% to as high as 35.5% across hospital units, and resistance rates at the Department of Urology have been shown to be significantly higher compared to other hospital units [14]. Resistance rates of in- and outpatients at our hospital ranged from 0 to 40% in 2008 [unpublished internal report].

The goals of this study were (i) to determine resistance rates in outpatients and inpatients with UTIs, (ii) to assess prescribers' choices for empirical antibiotic therapy, and (iii) to identify risk factors for infections due to ciprofloxacin-resistant *E. coli* in patients at the Department of Urology of the University Hospital Zurich, Switzerland.

Methods

Setting

The University Hospital in Zurich, Switzerland, is an 861 beds tertiary care teaching hospital. 36 beds are assigned to the Department of Urology. 1722 patients were admitted in 2006, accounting for 10412 bed-days (day of admission and day of discharge counted together as one bed-day) and a mean length of stay of 6.0 days. In the same year, 6514 patients were treated in the outpatient unit.

Patients

We performed a cross sectional study at the Department of Urology. All adult inpatients and outpatients were included in whom *E. coli* was isolated from clinical urinary samples or blood cultures (in case of clinical symptoms suggestive of urinary tract infection but negative urinary culture) in the study period from January 1, 2006 to August 31, 2007. Most of the in- and outpatients presenting with complicated urinary tract infections to the University Hospital Zurich are treated at the Department of Urology, except kidney transplant recipients. At our hospital, acute, uncomplicated urinary tract infections and women with acute, uncomplicated pyelonephritis are treated at the Department of Urology, the Department of Gynecology and Obstetrics, and at the Medical Emergency Department.

All specimens were tested in a central clinical microbiology laboratory (Institute of Medical Microbiology, University of Zurich). Bacteria were isolated from urine and blood cultures according to standard methods [15]. Antimicrobial susceptibility testing and screening for extended spectrum beta-lactamase (ESBL) was performed according to the Clinical and Laboratory Standards Institute (CLSI) [16]. Briefly, in the disk diffusion test, ciprofloxacin zone diameters of <15 mm and of >21 mm were considered resistant and susceptible, respectively; zones of 16–20 mm were considered as intermediately susceptible but were categorised as non-susceptible. Some strains were tested by a commercial microdilution test (Vitek2, BioMérieux, Marcy L'Étoile, France); minimal inhibitory concentrations (MIC) of ciprofloxacin of <1 mg/L and of >4 mg/L were considered susceptible and resistant, respectively; an MIC of 2 mg/L was intermediately susceptible but was categorised as non-susceptible. The screening test for ESBL was an inhibition zone of <22 mm against ceftazidime or of <27 mm against cefotaxime. Any synergy between amoxicillin/clavulanic acid and ceftazidime or cefepime (double disk method), or between piperacillin/tazobactam and cefotaxime in the disk diffusion test was also an indication for a confirmation test by Etest according to the prescription of the manufacturer (AB Biodisk, Solna, Sweden); a greater than twofold concentration decrease in an MIC for ceftazidime or cefepime, or for cefotaxime tested in combination with clavulanic acid versus its MIC when tested alone was confirmatory for ESBL. In accordance with the CLSI guidelines, all ESBL-producing *E. coli* strains were classified as resistant to all penicillins, cephalosporins and aztreonam regardless of the MICs determined for these drugs [16].

Demographic and clinical information of both in- and outpatients was collected from each patient by chart review using a structured questionnaire.

Definitions

Bacterial counts with 10^4 colony forming units or more per millilitre of urine in asymptomatic patients were considered to represent asymptomatic bacteriuria. Acute, uncomplicated urinary tract infection was defined as symptomatic cystitis, characterised by frequency, dysuria, suprapubic pain and urgency in women with a normal urogenital tract. In men, symptomatic urinary tract infections were classified as complicated. Acute, uncomplicated pyelonephritis was defined as a parenchymatous infection of the kidney in women with normal urogenital tract who presented with flank pain and often fever. Complicated urinary tract infection was defined as symptomatic cystitis or pyelonephritis in men or women with functional or structural abnormalities of the urogenital tract. Any detection of *E. coli* in blood culture samples was considered significant bacteremia. Infections were considered nosocomial if the patient was hospitalised in an acute care centre for >48 hours prior to sample collection. One antibiotic course was defined as administration of at least one dose of any antibacterial agent. A time interval of >24 hours between the administration of two doses was defined to separate one course from another, unless certain conditions (e.g. renal insufficiency) justified a dose interval of >24 hours. The variable 'recurrent UTIs' was recorded according to the available information from patient history without definition of a threshold.

Calculation of the Chronic Disease Score was performed according to McGregor et al. [17].

Statistical analysis

We used Stata (Version 10, StataCorp, College Station, Texas) for statistical analyses. Differences in group proportions were assessed by the Chi-square or Fisher's exact test, and differences in medians were calculated with the Wilcoxon rank-sum test. Logistic regression analysis was performed to identify risk factors for acquisition of fluoroquinolone-resistant *E. coli*. In multivariable analysis, male gender and all variables revealing a *p value* <0.2 in univariable analysis were included. A *p value* <0.05 was considered statistically significant.

Ethics approval

The study was approved by the local ethics committee.

Results

Patients and antibiotic prescriptions

275 patients were enrolled and a total of 345 urinary or blood culture samples were analysed. Patients' characteristics, clinical presentation and microbiological findings are summarised in table 1. The median age (interquartile range (IQR)) of the 151 (55%) women and the 124 (45%) men was 56.8 (51.9–60.4) years. Of the population studied, 178 (65%) subjects were treated as outpatients and 97 (35%) as inpatients. The most common diagnosis was acute, uncomplicated UTI (80 (29%) patients), followed by complicated UTI (69 (25%) patients). Ciprofloxacin-resistant *E. coli* was isolated in 61 patients, representing 36% of all inpatients and 15% of outpatients.

174 out of 286 (60.8%) initial antibiotic prescriptions were for fluoroquinolones, 13% were for penicillins and 7% were for sulfamethoxazole-trimethoprim. Fluoroquinolones were the empiric antibiotic therapy of choice in 72.5% (58/80) of all acute, uncomplicated urinary tract infections, in 76.5% (13/17) of all episodes of acute, uncomplicated pyelonephritis and in 65.0% (52/80) of all complicated urinary tract infections. Penicillins accounted for 10.0%, 17.6% and 16.3%, respectively, and sulfamethoxazole-trimethoprim accounted for 12.5%, 5.9% and 8.8%, respectively.

Predictors of ciprofloxacin-resistant *E. coli*

The characteristics of patients with ciprofloxacin-resistant strains were compared with those of patients with a ciprofloxacin-susceptible strain (table 2). Significant predictors of ciprofloxacin-resistant *E. coli* in univariable analysis were inpatient status, recurrent UTIs, urolithiasis, foreign material (e.g. pigtail catheter) in the upper urinary tract, urinary catheter, prior use of fluoroquinolones, prior use of any antibiotics and prior treatment in the Department of Urology. To identify independent risk factors, a multivariable analysis was performed. Thereby, fluoroquinolone use in the preceding year (odds ratio [OR] (95% confidence intervals [CI]): 2.24 (1.08–4.62), $p = 0.030$), urinary tract catheterisation in the preceding year (OR: 2.41 (1.02–5.67), $p = 0.044$) and recurrent urinary tract infections (OR: 2.26 (1.07–4.78), $p = 0.032$) were found to be independently associated with infection or colonisation with a ciprofloxacin-resistant strain.

A further analysis of prior antibiotic use is depicted in table 3. Only one cycle of fluoroquinolone treatment in the preceding year significantly increased the odds of being infected or colonised with a ciprofloxacin-resistant *E. coli* strain (OR: 2.80 (1.51–5.22), $p <0.001$), whereas one cycle of any antibiotic in the prior 12 months did not (OR: 1.36 (0.73–2.53), $p = 0.339$). However, the odds were significantly increased when multiple antibiotic cycles were recorded (OR: 4.40 (2.36–8.20), $p <0.001$), regardless of the antibiotic class used.

Antibiotic susceptibility of *E. coli* resistant and susceptible to ciprofloxacin

The cumulative antibiograms of ciprofloxacin-resistant and ciprofloxacin-susceptible *E. coli* strains are shown in table 4. Of the 345 isolates, 94 (27%) were resistant to ciprofloxacin. Compared with susceptible strains, ciprofloxacin-resistant *E. coli* strains showed significantly increased resistance rates to all antimicrobials tested, except for piperacillin-tazobactam and carbapenems (meropenem and imipenem). Among ciprofloxacin-susceptible strains, resistance to ampicillin (28%), tetracycline (20%) and trimethoprim-sulfamethoxazole (16%) was most prevalent. Ciprofloxacin-resistant strains produced extended-spectrum beta-lactamases (ESBL) significantly more often than ciprofloxacin-susceptible strains ($p <0.0001$).

Discussion

The aim of this study was to identify risk factors for colonisation or infection with ciprofloxacin-resistant *E. coli* in patients treated at the Department of Urology of the University Hospital Zurich. Our analysis demonstrated that 22% of the population under study was infected or colonised with ciprofloxacin-resistant *E. coli*. Recurrent urinary tract infections, urinary catheterisation within the last 12 months and use of fluoroquinolones in the last 12 months turned out to be independently associated with ciprofloxacin-resistant strains. Those resistant strains were often also resistant to other antibiotics, mostly against ampicillin (90%) and tetracyclin (72%). Fluoroquinolones turned out to be the most frequently prescribed antibiotics for treatment of acute uncomplicated UTI, acute uncomplicated pyelonephritis and complicated UTI.

Our study documents risk factors for UTIs caused by ciprofloxacin-resistant *E. coli* in patients at a tertiary care urology centre. The population studied is exceptional in respect to the high prevalence of diseases that facilitate urinary tract infections, for example urinary tract obstructions, or foreign material in the upper and lower urinary tract. The study has several limitations. Internal validity may be reduced, as measurement bias might have been introduced by collecting demographic and medical information by chart review. Charts of outpatients are usually not as detailed as those of inpatients, probably accounting for systematic deviations in the availability of information. Recall bias might have been introduced as patients with underlying urinary tract disorders might more appropriately report their antibiotic treatment history. In outpatients, antibiotic therapy for UTI is usually started empirically and cultures are only performed if the patient fails to respond to treatment,

has recurrent episodes of UTI or has complicated UTI [18, 19]. Thus, data on resistance rates based on laboratory surveillance may overestimate the true levels of antibiotic resistance in the community, accounting for selection bias. However, since most urinary samples obtained at the Department of Urology are sent for bacterial culture, the 22% resistance rate of *E. coli* to ciprofloxacin is likely to be a realistic number for the population under study. Generalisation of these results may be restricted as these data were collected in a single hospital department in one geographic area during an 18 months period. The odds ratios may be different in other settings, even within Switzerland.

Risk factors for ciprofloxacin-resistant *E. coli* in UTIs have been presented by other authors [9–13]. The results of our study are in agreement with risk factors previously reported, with prior exposure to fluoroquinolones being the most commonly described factor to increase risk. Whereas other authors tried to find an association with the presence of a urinary catheter at the time of detection of the ciprofloxacin-resistant strain [11, 12], we included prior ur-

Table 1
Patient characteristics.

Characteristic	Susceptibility *of E. coli* to ciprofloxacin		*p* value
	Susceptible, n (%)	Resistant, n (%)	
Total number of patients	214 (100)	61 (100)	
Female	121 (57)	30 (50)	0.312
Male	93 (43)	31 (51)	0.312
Age, median (95% CI)	55.5 (49.2–58.1)	63.8 (54.0–70.0)	0.062
Setting			
Outpatients	152 (71)	26 (43)	<0.001
Inpatients	62 (29)	35 (57)	<0.001
Length of stay, days, median (95% CI)	4 (4–6)	7 (5–10)	0.094
Chronic Disease Score, median (95% CI)	4.7 (3–5.5)	3 (3–4)	0.083
Clinical presentation			
Asymptomatic bacteriuria	41 (19)	12 (20)	1.000
Asymptomatic bacteriuria with indwelling catheter	18 (8)	9 (15)	0.148
Acute, uncomplicated urinary tract infection	74 (35)	6 (10)	<0.001
Acute, uncomplicated pyelonephritis	16 (7)	1 (2)	0.132
Complicated urinary tract infection	52 (24)	28 (46)	0.002
Bacteremia	0 (0)	1 (2)	0.222
Other/unclear diagnosis	13 (6)	4 (7)	1.000

Table 2
Risk factors for urinary tract infections with ciprofloxacin-resistant *E. coli*.

Variable	Susceptibility *of E. coli* to ciprofloxacin		Univariable analysis		Multivariable logistic regression analysis	
	Susceptible, n (%)	Resistant, n (%)	OR (95% CI)	*p* value	OR (95% CI)	*p* value
Number of patients	214 (100)	61 (100)				
Male gender	93 (43)	31 (51)	1.34 (0.76–2.38)	*0.309*	1.57 (0.77-3.17)	*0.212*
Age >65 years	78 (36)	29 (48)	1.58 (0.89–2.81)	*0.119*	1.00 (0.50-2.01)	*0.995*
In-hospital treatment	62 (29)	35 (57)	3.30 (1.83–5.94)	*<0.001*	1.98 (0.95-4.12)	*0.069*
Chronic Disease Score >3[1]	31 (50)	16 (46)	0.73 (0.32–1.70)	*0.470*		
Diabetes mellitus	15 (7)	3 (5)	0.69 (0.19–2.45)	*0.562*		
Malignoma, non-urological	4 (2)	1 (2)	0.88 (0.10–7.98)	*0.906*		
Malignoma, urological	18 (8)	10 (16)	2.14 (0.93–4.91)	*0.074*		
Nosocomial infection	4 (2)	1 (2)	0.88 (0.10–7.98)	*0.906*		
Recurrent urinary tract infection	73 (34)	33 (54)	2.28 (1.28–4.05)	*0.005*	2.26 (1.07–4.78)	*0.032*
Vesico-ureteral reflux	1 (0)	2 (3)	7.22 (0.64–81.01)	*0.109*	3.77 (0.28–50.43)	*0.316*
Benign prostatic hyperplasia[2]	25 (27)	9 (29)	1.30 (0.58–2.98)	*0.521*		
Urolithiasis	16 (7)	10 (16)	2.43 (1.03–5.67)	*0.040*	1.72 (0.61–4.85)	*0.303*
Urologic surgery in last 12 months[3]	41 (19)	27 (44)	3.35 (1.82–6.16)	*<0.001*		
Foreign material in upper urinary tract in last 12 months[3]	13 (6)	12 (20)	3.79 (1.63–8.81)	*0.002*		
Urinary catheter in last 12 months	39 (18)	33 (54)	5.29 (2.87–9.75)	*<0.001*	2.41 (1.02–5.67)	*0.044*
Fluoroquinoloneuse in last 12 months	49 (23)	36 (59)	4.85 (2.66–8.85)	*<0.001*	2.24 (1.08–4.62)	*0.030*
Use of other antibiotics in last 12 months	56 (26)	31 (51)	2.92 (1.62–5.25)	*<0.001*	1.59 (0.79–3.20)	*0.195*
Hospitalisation in Department of Urology in last 12 months	22 (10)	23 (38)	5.28 (2.68–10.43)	*<0.001*	1.28 (0.50–3.26)	*0.607*
Corticosteroids or other immunosuppressants in last 12 months	9 (4)	3 (5)	1.18 (0.31–4.49)	*0.810*		
Renal insufficiency	4 (2)	3 (5)	2.72 (0.59–12.48)	*0.199*	1.97 (0.32–12.06)	*0.464*
Kidney transplant recipient	1 (0)	1 (2)	3.55 (0.22–57.60)	*0.373*		
HIV infection	3 (1)	1 (2)	1.17(0.12–11.47)	*0.891*		

[1] inpatients, [2] in male patients, [3] these variables have been excluded in the multivariable analysis because of collinearity

inary tract catheterisation within one year as a possible risk factor. However, multivariable analysis did not reveal prior urinary tract catheterisation as an independent risk factor. In contrast, Arslan et al. found an association between ciprofloxacin resistance and complicated UTIs, including those patients with urinary catheters in situ [10]. Others have been able to show a correlation between age (50 years and 65 years or older, respectively) and fluoroquinolone resistance [9–11], whereas we could not. Differences between studies may have arisen due to different settings, different populations under study, and, to some extent, disregard of collinearity and cocausality in multivariable analyses.

During the study period, local guidelines of the University Hospital Zurich recommended a three day course of norfloxacin or trimethoprim/sulfamethazol for the treatment of acute, uncomplicated UTI in young women, and a 5 day course in men. Ciprofloxacin was only recommended as a first-line agent in the treatment of uncomplicated acute pyelonephritis. The results of our study show that those recommendations were not followed properly, as ciprofloxacin turned out to be the most frequently prescribed antibiotic for treatment of acute, uncomplicated UTIs. The fact that ciprofloxacin is often given inappropriately is alarming. However, as there is no evidence that norfloxacin has a lower capacity than ciprofloxacin to select for fluoroquinolone resistant strains, it cannot be assumed that following the institutional guidelines would have resulted in a lower prevalence of fluoroquinolone resistant strains of *E. coli*. Naber et al. demonstrated that most participants (microbiologists, infectious disease clinicians and clinicians with an interest in the management of UTIs) underestimated fluoroquinolone use in the management of acute, uncomplicated lower UTI and that they considered the high level of usage to be inappropriate from a societal perspective (risk of increased resistance) [3]. This suggests that part of decreasing the usage of fluoroquinolones is to inform clinicians about their high prescription rate as they tend to underestimate their use and are sometimes not aware of the high selection pressure. In the study by Van Hees et al. about strategies to optimise the use of ciprofloxacin, it could be shown that the numbers of inappropriate prescriptions can be reduced and the quality of prescriptions improved by educational interventions [20]. Similar investigations by Feucht et al. demonstrated that education of physicians resulted in an increase in appropriate empiric antibiotic use, a decrease in duration of inappropriate use, and a decrease in duplicate gram-negative coverage [21].

Across Europe, fluoroquinolone resistance rates show large differences, being generally high in southern Europe and low in northern European countries [6, 7]. These geographical variations are also seen in antibiotic consumption [4, 6, 22], which is being recognised as the main cause of emerging resistance [11, 23, 24]. Those international differences may be explained by different antimicrobial guidelines as well as cultural, demographic and socioeconomic factors, for instance, over-the-counter sales or physicians' and patients' attitudes to antibiotics. In 2002, Switzerland was the country with the lowest antibiotic consumption in the community in Europe. However,

Table 3
Antibiotic treatment within the previous 365 days.

	Susceptibility *of E. coli* to ciprofloxacin		**OR (95% CI)**	***p* value**
	Susceptible, n (%)	**Resistant, n (%)**		
Total number of patients	214 (100)	61 (100)		
No prior treatment	130 (61)	14 (23)	0.19 (0.10–0.37)	<0.001
Fluoroquinolones				
1 cycle	38 (18)	23 (38)	2.80 (1.51–5.22)	0.001
>1 cycle	11 (5)	13 (21)	5.00 (2.15–11.64)	<0.001
All antibiotics				
1 cycle	51 (24)	19 (31)	1.36 (0.73–2.53)	0.339
>1 cycle	33 (15)	28 (46)	4.40 (2.36–8.20)	<0.001

Table 4
Cumulative antibiograms of 345 *E. coli* isolates from 275 patients.

Variable	**Susceptibility *of E. coli* to ciprofloxacin**		***p* value**
	Susceptible, n (%)	**Resistant, n (%)**	
Ciprofloxacin	251 (100)	94 (100)	
Amoxicillin-clavulanate	6 (2)	17 (18)	<0.001
Ampicillin	71 (28)	83 (90)	<0.001
1st generation Cephalosporins	9 (4)	27 (29)	<0.001
Gentamicin	3 (1)	39 (41)	<0.001
Piperacillin-tazobactam	5 (2)	4 (4)	0.262
Sulfamethoxazole and trimethoprim	39 (16)	57 (62)	<0.001
Tetracycline	50 (20)	66 (72)	<0.001
Tobramycin	3 (1)	18 (20)	<0.001
Ceftazidime	3 (1)	12 (13)	<0.001
Ceftriaxone	1 (0)	12 (13)	<0.001
Meropenem	5 (2)	0 (0)	0.329
Imipenem	0 (0)	0 (0)	n.a.
Extended-Spectrum Beta-Lactamase producing strain	1 (0)	10 (11)	<0.001

fluoroquinolones accounted for a share of 20.1% thereof, which is a much higher proportion compared to an average of 7.3% in the other European countries [25]. Although antibiotic consumption in our country is still considered to be low, continuous monitoring of resistance development is essential to adapt guidelines for empirical antimicrobial therapy. In 2008, according to the SEARCH database (Sentinel Surveillance of Antibiotic Resistance in Switzerland), the rate of non-susceptible *E. coli* to older fluoroquinolones in urogenital infections of inpatients and outpatients aged ≥15 years reached 17.2% and 17.1%, respectively [26].

To halt the process of resistance development, susceptibility testing to first-generation fluoroquinolones (e.g. nalidixic acid) may be considered, as they indicate single mutation in the gyrA-gene whereof at least two are needed to provide relevant resistance to later generation fluoroquinolones [27–29]. It has previously been suggested that selection pressure could be reduced by refraining from fluorquinolone use when resistance to nalidixic acid is detected in order to decelerate the accumulation of single mutations [11, 27, 29]. Nonetheless, resistance of *E. coli* is not only selected by the use of fluoroquinolones, but also by the use of unrelated antimicrobial classes including ampicillin, amoxicillin, trimethoprim or sulfamethoxazole alone, and trimethoprim-sulfamethoxazole [7]. Therefore, to decrease selection pressure to those 'classic' antibiotics, more frequent use of other antibiotics, for example nitrofurantion and fosfomycin, may be considered. In complicated UTIs, microbiological testing is essential to ensure adequate therapy because of high resistance rates.

Funding / potential competing interests

The authors declare no financial or commercial conflict of interest.

References

1 Foxman B, Brown P. Epidemiology of urinary tract infections: transmission and risk factors, incidence, and costs. Infect Dis Clin North Am. 2003;17(2):227–41.

2 Gupta K, Hooton TM, Stamm WE. Increasing antimicrobial resistance and the management of uncomplicated community-acquired urinary tract infections. Ann Intern Med. 2001;135(1):41–50.

3 Naber KG. Survey on antibiotic usage in the treatment of urinary tract infections. J Antimicrob Chemother. 2000;46(Suppl A):49–52.

4 Cars O, Molstad S, Melander A. Variation in antibiotic use in the European Union. Lancet. 2001;357(9271):1851–3.

5 Ena J, Lopez-Perezagua MM, Martinez-Peinado C, Cia-Barrio MA, Ruiz-Lopez I. Emergence of ciprofloxacin resistance in Escherichia coli isolates after widespread use of fluoroquinolones. Diagn Microbiol Infect Dis. 1998;30(2):103–7.

6 Goossens H, Ferech M, Vander Stichele R, Elseviers M. Outpatient antibiotic use in Europe and association with resistance: a cross-national database study. Lancet. 2005;365(9459):579–87.

7 Kahlmeter G. An international survey of the antimicrobial susceptibility of pathogens from uncomplicated urinary tract infections: the ECO.SENS Project. J Antimicrob Chemother. 2003;51(1):69–76.

8 Kresken M, Hafner D, Mittermayer H, Verbist L, Bergogne-Berezin E, Giamarellou H, et al. Prevalence of fluoroquinolone resistance in Europe. Study Group "Bacterial Resistance" of the Paul-Ehrlich-Society for Chemotherapy e. V. Infection. 1994;22(Suppl 2):S90–8.

9 Alos JI, Serrano MG, Gomez-Garces JL, Perianes J. Antibiotic resistance of Escherichia coli from community-acquired urinary tract infections in relation to demographic and clinical data. Clin Microbiol Infect. 2005;11(3):199–203.

10 Arslan H, Azap OK, Ergonul O, Timurkaynak F. Risk factors for ciprofloxacin resistance among Escherichia coli strains isolated from community-acquired urinary tract infections in Turkey. J Antimicrob Chemother. 2005;56(5):914–8.

11 Ena J, Amador C, Martinez C, Ortiz de la Tabla V. Risk factors for acquisition of urinary tract infections caused by ciprofloxacin resistant Escherichia coli. J Urol. 1995;153(1):117–20.

12 Killgore KM, March KL, Guglielmo BJ. Risk factors for community-acquired ciprofloxacin-resistant Escherichia coli urinary tract infection. Ann Pharmacother. 2004;38(7-8):1148–52.

13 Sotto A, De Boever CM, Fabbro-Peray P, Gouby A, Sirot D, Jourdan J. Risk factors for antibiotic-resistant Escherichia coli isolated from hospitalized patients with urinary tract infections: a prospective study. J Clin Microbiol. 2001;39(2):438–44.

14 Kuster SP, Ruef C, Zbinden R, Gottschalk J, Ledergerber B, Neuber L, et al. Stratification of cumulative antibiograms in hospitals for hospital unit, specimen type, isolate sequence and duration of hospital stay. J Antimicrob Chemother. 2008;62(6):1451–61.

15 Clarddige JE, Johnson JR, Pezzlo M. Laboratory diagnosis of urinary tract infections. Cumitech 3B. American Society for Microbiology, Washington, D.C. Cumitech 3B American Society for Microbiology, Washington, DC. 1998.

16 Clinical and Laboratory Standards Institute. 2008. Performance Standards for Antimicrobial Susceptibility Testing; Eigtheenth Informational Supplement 100-S18. Clinical and Laboratory Standards Instiute, Wayne, PA, USA.

17 McGregor JC, Kim PW, Perencevich EN, Bradham DD, Furuno JP, Kaye KS, et al. Utility of the Chronic Disease Score and Charlson Comorbidity Index as comorbidity measures for use in epidemiologic studies of antibiotic-resistant organisms. Am J Epidemiol. 2005;161(5):483-93.

18 Ti TY, Kumarasinghe G, Taylor MB, Tan SL, Ee A, Chua C, et al. What is true community-acquired urinary tract infection? Comparison of pathogens identified in urine from routine outpatient specimens and from community clinics in a prospective study. Eur J Clin Microbiol Infect Dis. 2003;22(4):242–5.

19 Richards DA, Toop LJ, Chambers ST, Sutherland MG, Harris BH, Ikram RB, et al. Antibiotic resistance in uncomplicated urinary tract infection: problems with interpreting cumulative resistance rates from local community laboratories. N Z Med J. 2002;115(1146):12–4.

20 van Hees BC, de Ruiter E, Wiltink EH, de Jongh BM, Tersmette M. Optimizing use of ciprofloxacin: a prospective intervention study. J Antimicrob Chemother. 2008;61(1):210–3.

21 Feucht CL, Rice LB. An interventional program to improve antibiotic use. Harvey Whitney Books; 2003. p. 646–51.

22 Kahlmeter G, Menday P, Cars O. Non-hospital antimicrobial usage and resistance in community-acquired Escherichia coli urinary tract infection. J Antimicrob Chemother. 2003;52(6):1005–10.

23 Goettsch W, van Pelt W, Nagelkerke N, Hendrix MG, Buiting AG, Petit PL, et al. Increasing resistance to fluoroquinolones in escherichia coli from urinary tract infections in the netherlands. J Antimicrob Chemother. 2000;46(2):223–8.

24 Gagliotti C, Nobilio L, Moro ML. Emergence of ciprofloxacin resistance in Escherichia coli isolates from outpatient urine samples. Clin Microbiol Infect. 2007;13(3):328–31.

25 Filippini M, Masiero G, Moschetti K. Socioeconomic determinants of regional differences in outpatient antibiotic consumption: evidence from Switzerland. Health Policy. 2006;78(1):77–92.

26 anresis.ch – Sentinel Surveillance of Antibiotic Resistance in Switzerland [Internet]. University of Bern. c2005 – [cited 2009 Oct 10]. Available from: www.search.ifik.unibe.ch.

27 Baquero F. Resistance to quinolones in gram-negative microorganisms: mechanisms and prevention. Eur Urol. 1990;17(Suppl 1):3–12.

28 Vila J, Ruiz J, Marco F, Barcelo A, Goni P, Giralt E, et al. Association between double mutation in gyrA gene of ciprofloxacin-resistant clinic-

al isolates of Escherichia coli and MICs. Antimicrob Agents Chemother. 1994;38(10):2477–9.

29 Komp Lindgren P, Karlsson A, Hughes D. Mutation rate and evolution of fluoroquinolone resistance in Escherichia coli isolates from patients with urinary tract infections. Antimicrob Agents Chemother. 2003;47(10):3222–32.