J Infect Chemother 22 (2016) 478–482

Contents lists available at ScienceDirect

Journal of Infection and Chemotherapy

journal homepage: http://www.elsevier.com/locate/jic

Original article

Clinical analysis of bacterial strain profiles isolated from urinary tract infections: A 30-year study

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ARTICLE INFO

Article history:
Received 13 February 2016
Received in revised form
1 April 2016
Accepted 18 April 2016
Available online 20 May 2016

Keywords:
Urinary tract infection
Antibiogram
Antimicrobial susceptibility
Fluoroquinolone-insusceptible *Escherichia coli*

ABSTRACT

Objectives: We analyzed bacterial strains isolated from urine samples of patients with urinary tract infections (UTI) at Okayama University Hospital over a 30-year period to characterize trends in species and antimicrobial susceptibilities.

Methods: Clinical isolates were collected from in- and out-patients with pyuria and bacteriuria who were treated between 1984 and 2014 (one episode per patient and plural isolates were counted in polymicrobial infection). We examined these isolates to identify pathogens and tested for antimicrobial susceptibility.

Results: Isolates from complicated UTI over a 30-year period revealed *Pseudomonas aeruginosa* (*P. aeruginosa*) was the most frequently isolated in the first decade (1984–1994), MRSA in the second decade (1995–2004), and *Escherichia coli* (*E. coli*) in the latest decade (2005–2014). In uncomplicated UTI examined over 20 years, *E. coli* was the most frequently isolated species accounting for 47–94% of isolates. Fluoroquinolone (FQs)-insusceptible *E. coli* were first isolated in 1994 and increased to about 35% in 2013 in patients with complicated UTI.

Conclusions: Complicated UTI involving *P. aeruginosa* and MRSA decreased over the last 10 years. Our data suggest that several factors such as shorter hospitalizations, shorter indwelling catheter use, and appropriate antimicrobial use has decreased colonization of *P. aeruginosa* and MRSA with relative increases in isolation of *E. coli* including FQs-insusceptible strains.

We must continue our surveillance of antimicrobial-resistant bacteria isolated from urine samples and evaluate antibiograms, since their persistence in the urinary tract would be problematic.

1. Introduction

Pathogens isolated from urinary tract infection (UTI) showed specific tendencies in each decade and this reflects comprehensive healthcare practices and how practices have changed over the years. For example, mean hospitalization periods have been decreased as national policy [1] and guidelines for prevention of Catheter-Associated Urinary Tract Infections have recommended antimicrobial administration and duration of indwelling urinary catheter use should be minimized [2]. In addition, antimicrobials for treatment or prophylaxis of UTI are beginning to be selected and used appropriately in accordance with various guidelines [3,4]. As healthcare practices change over time, it is extremely important to create antibiograms for each decade by surveying antimicrobial susceptibilities of clinical isolates from urine samples. Antibiograms will help prevent nosocomial infections and ensure the appropriate use of antimicrobial agents. At the Department of Urology in Okayama University Hospital, the surveillance of bacterial isolates and drug susceptibility profiles has been continued

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http://dx.doi.org/10.1016/j.jiac.2016.04.004
1341-321X/

for over 30 years. We would like to report our long-term results on how these isolates have changed over time, and address the issue of fluoroquinolone (FQs) susceptibility in *Escherichia coli* (*E. coli*), a major source of concern in recent years.

2. Materials and methods

The subjects were patients with complicated UTI who were seen at the outpatient clinic or ward of the Urology Clinic of Okayama University Hospital between 1984 and 2014 and patients with uncomplicated UTI between 1994 and 2014. The patients with pyuria (WBC ≥5/HPF) and bacteriuria (bacteria $\geq 1.0 \times 10^4$ CFU/ml in midstream urine or $\geq 1.0 \times 10^3$ CFU/ml in catheterized specimen) were included in this study. Isolates were counted by one infectious episode per patients and plural isolates were counted in polymicrobial infection.

The minimum inhibitory concentrations (MIC) of various antimicrobials have been measured using broth microdilution method according to the guidelines published between 1990 (approved standard-second edition [5]) and 2012 (approved standard-ninth edition [6]) by the Clinical Laboratory Standards Institute (CLSI). The antimicrobial agents for which the MICs were measured were piperacillin (PIPC), cefazolin (CEZ), cefozopran (CZOP), imipenem (IPM), levofloxacin (LVFX), and gentamicin (GM). The criterion for definition of FQs-insusceptible *E. coli* strains was changed from ofloxacin (OFLX) MICs ≥4 μg/mL (until 2006) to LVFX MICs ≥4 μg/mL (from 2007) according to guidelines published by CLSI in 2007 [7]. This retrospective study was approved by ethics committee of Okayama University Hospital (Registration no. 1968).

3. Results

3.1. Urinary isolates in complicated UTIs in the past 30 years

Profiles of bacterial strains isolated from complicated UTI between 1984 and 2014 are shown in Fig. 1. The most interesting and remarkable tendency of isolation rates were observed in regard to *Pseudomonas aeruginosa* (*P. aeruginosa*), MRSA and *E. coli*. Isolation rates for *P. aeruginosa* (median (range)) were 20.2% (15.1–25.1%) in the first decade, 10.7% (6.4–20.6%) in the second decade and 6.0% (3.2–14.3%) in the latest decade revealing a marked decrease over time. MRSA isolates were first confirmed in our department in 1990, and gradually increased until 2007 (10.3%) but recently account for around 3%. *E. coli* isolation rates (median (range)) were 10.3% (4.8–14.3%) in the first decade, 16.3% (12.7–19.8%) in the second, and 23.4% (19.0–27.8%) in the latest decade. Isolation rates tended to increase over the last ten years.

3.2. Isolates from uncomplicated UTI in the past 20 years (1994–2014)

Profiles of all uncomplicated UTI isolates collected during the past 20 years are shown in Fig. 2. *E. coli* was the most frequently isolated pathogen and implicated in 47–94%. Isolates of gram-negative rods (GNR) except *E. coli* (e.g. *P. aeruginosa*, *Proteus* spp., and *Serratia* spp.) and gram-positive cocci (GPC) including *Enterococcus faecalis* (*E. faecalis*) and MRSA were uncommon in uncomplicated UTI.

3.3. Annual changes of FQs-insusceptible E. coli

Fig. 3 shows the number of FQs-insusceptible *E. coli* strains and percentages accounted for by resistant *E. coli* strains over time. FQs-insusceptible *E. coli* was first isolated in 1994 and although its incidence has fluctuated, overall, these resistant strains have shown a tendency to increase and over 25 strains were isolated in 2013. FQs-insusceptible *E. coli* strains were counted according to underlying diseases since 2004. A total of 190 strains of FQs-insusceptible *E. coli* strains were isolated, and 165 of 190 strains (86.8%) were isolated from complicated UTI. Furthermore, in patients with complicated UTI, the rate of FQ-insusceptible *E. coli* strains in all the *E. coli* strains have been over 30% since 2011.

3.4. E. coli antimicrobial susceptibility

The MICs of *E. coli* strains isolated between 2004 and 2014 to various antibacterial agents were measured. While susceptibilities to IPM and GM are preserved, susceptibilities to PIPC, CEZ, CZOP and OFLX/LVFX have shown a tendency to decrease over time. Especially, susceptibility to OFLX/LVFX has the most remarkably deteriorated every year; 93.4% of *E. coli* strains were susceptible in 2002, but susceptible strains had decreased to 62.8% of all *E. coli* in 2011.

According to strains isolated from 2004 to 2014, differences of cumulative percentage MIC distributions between *E. coli* strains isolated from complicated UTI and uncomplicated UTI are shown in Fig. 4. Compared to the *E. coli* strains isolated uncomplicated UTI, those isolated from complicated UTI expressed decreased susceptibility to PIPC, CEZ, CZOP, and LVFX, although it remained sensitive to only IPM and GM.

4. Discussion

The long-term result of a 30-year surveillance of urinary isolates and their drug susceptibilities over time was reported. In uncomplicated UTI examined for over 20 years, *E. coli* was the most common bacteria among urinary isolates. In complicated UTI, 40% of isolates were gram-positive bacteria which included *E. faecalis* and MRSA, while *E. coli* and *Klebsiella pneumoniae* were the most common gram-negative bacterial isolates. In a 30-year surveillance of urinary isolates in complicated UTI, the only notable tendencies were as follows: *P. aeruginosa* tended to be the most prevalent during the first decade (1984–1994), MRSA during the second decade (1995–2004), and *E. coli* in the latest decade (2005–2014), respectively.

There are only a few published reports on the surveillance of clinical isolates and their antibiograms at various medical facilities [8–10], but *E. coli* is generally the most commonly isolated pathogen in uncomplicated UTIs. In complicated UTIs, *P. aeruginosa* and MRSA are isolated more frequently [8,9]. Our investigation showed tendencies similar to these reports with no notable differences.

Changes in urinary isolate profiles in complicated UTIs during this 30-year period revealed that the isolation rates of *P. aeruginosa*, MRSA, and *E. coli* were the most common pathogens in the initial, second, and third decades, respectively. Why did isolation rates for *P. aeruginosa* and MRSA decrease, while *E. coli*, most commonly isolated and cultured from rectal isolates, have relatively increased? In our department, hospitalization period especially for urological operation have been shortened (data from 2006 were available; Fig. 5) since guidelines about indwelling catheters and antimicrobials have been abided. Namely, we believe improvements in healthcare such as shorter hospital stays [1], limiting use of indwelling catheters as recommended by various guidelines [2], appropriate use of antibiotics [3,4], and measures to prevent nosocomial infections have all contributed to these results.

FQs-insusceptible *E. coli* is becoming an issue not only in Japan [8–12], but also in other countries of the world [13–16]. It is implicated in 2.3–13.3% of uncomplicated UTIs, and in an even higher percentage of complicated UTIs or 12.8%–32.5%. According to reports, resistant strains account for as much as 14.7–30% of all