The Bacterial Spectrum and Antimicrobial Susceptibility in Female Recurrent Urinary Tract Infection: How Different They Are From Sporadic Single Episodes?

Marcelo Hisano, Homero Bruschini, Antonio Carlos Nicodemo, Cristiano Mendes Gomes, Marcos Lucon, and Miguel Srougi

OBJECTIVE To analyze and compare the etiological uropathogens and the susceptibility profile findings on urine culture between sporadic cases of community-acquired, uncomplicated urinary tract infection (UTI) and recurrent UTI cases in women.

MATERIALS AND METHODS We retrospectively analyzed the clinical data of 1629 women with uncomplicated UTI evaluated at our hospital between January 2007 and December 2012. Patients were divided into 2 groups: (1) no recurrent UTI and (2) recurrent UTI. We analyzed the microbiological findings and compared susceptibility profiles between groups.

RESULTS A total of 420 women were included. Group 1 had 233 (55.5%) patients and group 2 had 187 (44.5%). *Escherichia coli* was the most common agent in both groups (76.4% and 74.3%, respectively; $P = .625$), whereas *Staphylococcus saprophyticus* (8.2%) was the second most common in group 1, and *Enterococcus faecalis* was the second most common in group 2 (8.0%). Nitrofurantoin was the only oral agent that maintained the susceptibility profile in both groups (87.1% and 88.7%, respectively; $P = .883$). For *E coli* infections, only nitrofurantoin and amoxicillin/clavulanate maintained susceptibility rates more than 90% in both groups.

CONCLUSION UTI episodes in patients with recurrent UTI had similar bacterial spectra, but different susceptibility profiles compared with those from patients with nonrecurrent infections. The susceptibility rate for nitrofurantoin in patients with recurrent UTI remained high and comparable to the observed in patients with sporadic UTI, reinforcing its indication for empirical treatment while waiting for urine culture results. UROLOGY 86: 492–497, 2015. © 2015 Elsevier Inc.

Urinary tract infection (UTI) in women is a prevalent disease and can be classified as uncomplicated or complicated.[1,2] Uncomplicated UTI occurs in normal patients without structural or functional abnormalities, who are not pregnant and have not been recently subjected to surgical procedures.[2,3] According to location, they can be divided into lower (cystitis) and upper (pyelonephritis) urinary tract infections.[4,5]

Guidelines recommend the use of empirical antibiotic for the treatment of uncomplicated UTI, without microbiological confirmation.[5,6] This treatment follows established clinical guidelines, periodically updated by microbiological surveillance studies.[7-9] Despite the usually high successful treatment rates of uncomplicated female UTI (>90%),[6] recurrence occurs in up to 60% of patients during the first year[10]; therefore, recurrent UTI is a common phenomenon in women. There are many recurrence prevention strategies in the literature and also recommended by guidelines.[3,5,11] However, there is scant information in the literature about the flora and antibiotic profile susceptibility of UTI-recurrent episodes in these patients.[12,13]

The goals of this study were to analyze and compare the microbiological findings and the antimicrobial susceptibility profile of UTI in patients with and without recurrent UTI and to identify antimicrobial options for the empirical treatment of recurrent UTI episodes while waiting for urine culture results.

Financial Disclosure: *The authors declare that they have no relevant financial interests.*

From the Division of Urology, Hospital das Clínicas, University of São Paulo, Brazil; and the Department of Infectious Disease, Hospital das Clínicas, University of São Paulo, Brazil

Address correspondence to: Homero Bruschini, M.D., 255, University of São Paulo, Dr Eneas de Carvalho Aguiar Avenue, 7th floor, 05403-001 São Paulo, SP, Brazil. E-mail: bruschini@uol.com.br

Submitted: March 17, 2015, accepted (with revisions): May 9, 2015

http://dx.doi.org/10.1016/j.urology.2015.05.033
0090-4295/15

MATERIALS AND METHODS

Between January 2007 and December 2012, we reviewed the clinical records of 1629 female patients aged ≥14 years who were seen in our University Hospital with the diagnosis of UTI,[14] either from Urological Emergency Department and Urological Office. Only patients who had symptomatic, community-acquired episodes of acute cystitis or acute pyelonephritis were included. In addition, based on clinical history and available radiological tests, patients should have no serious comorbidities, structural or functional abnormalities within the urinary tract, including kidney stones >5 mm, any ureteral or bladder stones, a UTI episode <1 month before the current episode, recent urinary catheterization, recent urologic surgery (<6 months), having a double-J stent, neurogenic bladder, urinary diversion, kidney transplantation, or any congenital urologic abnormality without correction and pregnancy. We excluded patients who were unable to confirm the presence or absence of previous recurrent UTI and those with negative urine cultures despite clinical symptoms. This study had the approval of the Institutional Ethical Committee.

Uncomplicated cystitis was defined as including clinical symptoms of dysuria, frequency, urgency, and suprapubic pain, with or without hematuria. Uncomplicated pyelonephritis was defined as the clinical symptoms of flank pain, associated with nausea, vomiting, and fever (>37.8°C), with or without symptoms of cystitis, but with no signs of sepsis, no surgical treatment required, and no necessity of intensive care hospitalization. Because of the unknown status of local microbiota and susceptibility profile, all patients had a midstream clean catch urine culture from the first morning voiding or at least 2 hours from the last micturition, just after clinical diagnosis. The specimen was conditioned sterile in air temperature and sent to the laboratory in <2 hours. Urine cultures were analyzed, and a colony count of ≥1000 colony-forming unit/mL was considered to be positive in cases of symptomatic cystitis and ≥10,000 colony-forming unit/mL in cases of pyelonephritis. These thresholds were considered, according to the European Guidelines on Urological Infections,[5] because all cases had clinical symptoms of UTI. The identification of isolates and susceptibility tests were performed on VITEK 1 and 2 automated systems (bioMérieux, Marcy-l'Étoile, France). When we identified mixed infections (the presence of 2 bacteria), each agent was counted as 1 and analyzed separately. The minimal inhibitory concentration of antimicrobials was determined, and strains were considered to be susceptible, intermediately susceptible, or resistant according to the breakpoints determined by the Clinical and Laboratory Standards Institute[15] at the time of the analysis. The following antimicrobials were tested: amikacin, amoxicillin/clavulanate (A/C), ampicillin, cefepime, cefotaxime, cefoxitin, ceftazidime, cephalothin, ciprofloxacin, gentamicin, levofloxacin, nalidixic acid, nitrofurantoin, norfloxacin, piperacillin/tazobactam (P/T), and sulfamethoxazole/trimethoprim. The susceptibility profile of selected bacteria such as *Staphylococcus saprophyticus*, *Streptococcus agalactiae*, and others coagulase-negative *Staphylococcus* was not tested routinely.

Recurrent UTI was defined as the occurrence of 2 or more UTI episodes during a period of 6 months,[4,16] including the current analyzed episode. The recurrent episode occurred between 1 and 6 months after the first episode. Because of the retrospective nature of this study, we did not have reliable information about the treatment of all previous UTI episodes.

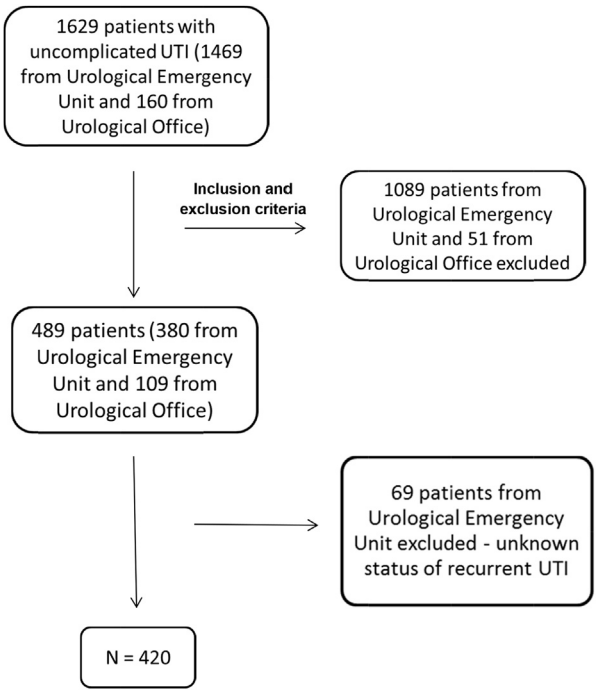

Figure 1. Flow chart for selection of patients for the study. UTI, urinary tract infection.

Patients were divided in 2 groups: group 1—patients without recurrent UTI and group 2—patients with recurrent UTI. Cases were analyzed and compared according to the microbiological findings of the patients' urine samples. We also compared the results for *Escherichia coli* infections in both groups and for the extended spectrum beta-lactamase (ESBL) production status.

Quantitative variables were described using means and ranges. Qualitative or categorical variables were described using their absolute values or proportions. Statistical analyses of the parametric results were performed by Student's *t* test, whereas for nonparametric results, chi-square test or likelihood ratio test was performed. When the samples were insufficient for chi-square analysis, the Fisher exact test was performed. Statistical significance was defined as $P < .05$. Data were processed using commercially available statistical software (SPSS Statistics version 20.0, IBM, Armonk, NY).

RESULTS

Of the 1629 patients initially analyzed, 420 patients met clinical criteria to be eligible for the study (Fig. 1). Group 1 had 233 patients (55.5%), and group 2 had 187 patients (44.5%). The mean ages (and ranges) of the patients in groups 1 and 2 were 39.5 years (16-96 years) and 48.6 years (14-85 years), respectively ($P < .0001$). In terms of the anatomical level of the uncomplicated UTI, group 1 had 172 (73.8%) cystitis and 61 (26.2%) pyelonephritis, whereas group 2 had 165 (88.2%) cystitis and 22 (11.8%) pyelonephritis ($P = .002$).

The isolated bacteria of both groups are summarized in Table 1. *E coli* was the most common agent isolated in both groups, with 76.4% and 74.3%, respectively. We did not find significant differences between the microbiological