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ORIGINAL ARTICLE

Changing antibiotic susceptibilities of community-acquired uropathogens in Greece, 2005—2010

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Purpose: The purpose of this study was to determine the distribution and changes in the antibiotic susceptibilities of uropathogens isolated from adults with community-acquired urinary tract infections (CA-UTIs) in Crete, Greece, over a 6-year period.
Methods: This study was performed with isolates from outpatients with UTIs, collected between 2005 and 2010. Isolates were identified by standard methods and antimicrobial susceptibility testing was performed using the disk diffusion method and the VITEK2 is an automated system used for identification and antimicrobial susceptibility testing of microorganisms (BioMerieux). To identify changes in susceptibility patterns, we compared results of the period 2005—2007 to those of the period 2008—2010. We also compared the antibiotic susceptibilities of isolates between males and females.
Results: A total of 4011 community-acquired uropathogens were isolated during the period of 2005—2010. *Escherichia coli* was the most common organism and responsible for 68.9% of CA-UTIs, followed by *Proteus mirabilis* (6.8%), *Klebsiella pneumoniae* (6.4%) and enterococci (6%). A significant increase in resistance of *E coli* isolates was noted for β-lactams, monobactams, aminoglycosides, quinolones, and cotrimoxazole. The reverse trend was evident for nitrofurantoin. Higher resistance rates of community-acquired *E coli* and non-*E coli* Enterobacteriaceae were noted in males for ampicillin, amoxicillin plus clavulanic acid, cephalosporins, aminoglycosides, and quinolones. No significant sex differences were noted in the antibiotic susceptibility patterns of enterococci.
Conclusion: There is a concerning trend for increasing resistance among *E coli* and non-*E coli* Enterobacteriaceae responsible for CA-UTIs in Crete in recent years likely due to the

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inappropriate use of broad spectrum antibiotics, as a substitute for precise diagnostics and/or to increase the chances of therapeutic success.

Introduction

To optimize the use of empirical antibacterial therapy for community acquired urinary tract infections (CA-UTIs), physicians should know the etiology and susceptibility patterns of urinary pathogens in their community.

Most CA-UTIs reflect episodes of acute, uncomplicated cystitis. The Infectious Diseases Society of America (IDSA) guidelines for the treatment of acute uncomplicated cystitis in women recommend the use of a 3-day course of cotrimoxazole as empiric first-line therapy except in communities with resistance rates exceeding 10%—20% to cotrimoxazole among uropathogens.[1] Although the relationship between antibiotic consumption and resistance is complex and some studies show no significant change in antimicrobial susceptibility over time,[2] increased antibiotic use and inappropriate use of newer broad spectrum antibiotics due to the fear of therapeutic failure with older agents, selects for resistant organisms, and antibiotic resistance is increasing among community-acquired urinary pathogens worldwide.[3—5]

The University Hospital of Heraklion is the only tertiary hospital in the island of Crete, Greece, and serves a population of more than 700,000 people. In this study, we describe the *in vitro* antimicrobial susceptibility patterns of community-acquired uropathogens that were isolated in the microbiology laboratory of this hospital over the period January 2005 to December 2010.

Materials and methods

Patients

The patients of this study were adult (age >14 years) outpatients of both sexes diagnosed and treated for CA-UTIs in one of the several outpatient clinics of the University Hospital of Heraklion. A UTI was considered as community-acquired if the patient had not received intravenous therapy or specialized wound care, had not received hemodialysis treatment or antineoplastic chemotherapy within the 30 days prior to infection, was not hospitalized in an acute care center the last 90 days before diagnosis of UTI, and did not reside in a nursing home or long-term care facility.[6] Patients with urinary catheters were excluded, since by definition they were considered as having healthcare-associated or nosocomial UTIs. All urine samples were collected in the emergency room or in one of the outpatient clinics of the hospital. Duplicate positive urine cultures, i.e., cultures from the same episode of UTI were excluded.

Laboratory methods

Quantitative urine cultures were performed with standard techniques using Columbia blood and MacConkey agar plates (BioMérieux, Marcy l' Etoile, France).[7] Plates were incubated for 18—24 hours at 36°C. Isolate identification was done by standard biochemical methods, the API system, and the VITEK2 automated system (BioMérieux). Antimicrobial susceptibility testing was performed using the disk diffusion method and the VITEK2 automated system.

The following antibiotics were tested against Gram-negative isolates: ampicillin, amoxicillin plus clavulanic acid (CA), ticarcillin, ticarcillin plus CA, piperacillin, piperacillin/tazobactam, cephalothin, cefoxitin, cefuroxime, cefotaxime, ceftriaxone, ceftazidime, cefepime, aztreonam, imipenem, tobramycin, amikacin, gentamicin, netilmicin, tetracycline, colistin, cotrimoxazole, nitrofurantoin, nalidixic acid, pefloxacin, ofloxacin, norfloxacin, and ciprofloxacin. Double-disk synergy test was used for preliminary classification of the isolates as extended-spectrum β-lactamase (ESBL) producers. The synergistic activity of CA with both ceftazidime and cefotaxime was confirmed by means of E-test special strips (AB Biodisk, Solna, Sweden) containing ceftazidime/ceftazidime plus CA and cefotaxime/cefotaxime plus CA.[8]

The following antibiotics were tested against enterococci: Ampicillin, ampicillin plus sulbactam, gentamicin [high level (HL) resistance], tetracycline, nitrofurantoin, ciprofloxacin, vancomycin, and teicoplanin. Quality control strains used for antimicrobial susceptibility testing included *E coli* ATCC 25922, *Pseudomonas aeruginosa* ATCC 27853, *K pneumoniae* ATCC 700603 (ESBL producer), and *Enterococcus faecalis* ATCC 29212. Results were interpreted according to the Clinical and Laboratory Standards Institute (CLSI) criteria.[8]

Statistical analysis

The proportion of resistant organisms was calculated by dividing the number of urinary isolates resistant to each antibiotic by the number of organisms that were tested against that antimicrobial agent. Intermediately resistant and resistant organisms were grouped together. To test for changes in the antibiotic susceptibilities of uropathogens over time, Fisher's exact test was used to compare the antibiotic susceptibilities of *E coli*, non-*E coli* Enterobacteriaceae, and *Enterococcus* spp. between the first (1/2005-12/2007) and second half of the study period (1/2008-12/2010), and between males and females. All tests were two-tailed and statistical significance was set at p values < 0.05. Statistical analysis was performed by Graphpad Prism software (version 4, La Jolla, CA, USA).

Results

A total of 4011 uropathogens were isolated during the period of January 2005 to December 2010 from patients with CA-UTIs. The distribution of urinary pathogens by