Enferm Infecc Microbiol Clin. 2018;36(7):417–422

Enfermedades Infecciosas y Microbiología Clínica

www.elsevier.es/eimc

Original article

Antimicrobial susceptibility of microorganisms that cause urinary tract infections in pediatric patients

Jesús Rodríguez-Lozano[a,*], Ana de Malet[a], María Eliecer Cano[a], Luis de la Rubia[b], Reinhard Wallmann[c], Luis Martínez-Martínez[d], Jorge Calvo[a]

[a] Servicio de Microbiología, Hospital Universitario Marqués de Valdecilla-IDIVAL, Santander, Spain
[b] Servicio de Pediatría, Hospital Universitario Marqués de Valdecilla, Santander, Spain
[c] Servicio de Medicina Preventiva, Hospital Universitario Marqués de Valdecilla, Santander, Spain
[d] Servicio de Microbiología, Hospital Universitario Reina Sofía, Córdoba, Spain

ARTICLE INFO

Article history:
Received 16 May 2017
Accepted 8 August 2017

Keywords:
Antimicrobial susceptibility
Pediatrics
Urinary tract infection
Cumulative susceptibility reports
Epidemiology

ABSTRACT

Introduction: Cumulative susceptibility reports are a valuable tool for the empirical treatment of urinary tract infections, especially in the current context of increasing resistance rates. Our objective was to analyze the antimicrobial susceptibility of bacterial isolates in urine cultures of pediatric patients during a five-year period.
Methods: Retrospective study of urine cultures from 2011 to 2015. Identification and antimicrobial susceptibility tests were performed using the Vitek-2 system (BioMérieux®) and categorized according to EUCAST criteria. Antimicrobial susceptibility data were analyzed by gender and age groups (neonates, 1 month to 5 years, 5–15 years) before being compared with data obtained from patients over the age of 15 years.
Results: During the study period, 17 164 urine cultures were processed from 7924 patients under 16 years of age. Antimicrobial susceptibility rates in these patients were: ampicillin 36.3%, amoxicillin/clavulanic acid 75.3%, cefuroxime 83.2%, co-trimoxazole 68.9%, ciprofloxacin 85.3%, fosfomycin 85.5%, nitrofurantoin 84.4% and 3rd generation cephalosporins 89–91%. Aminoglycosides (>92%) and carbapenems (95%) maintained the highest susceptibility rates. The prevalence of ESBL-producing isolates was significantly lower in children under the age of 16 years (1.5% vs. 4.1%). In patients under the age of 16 years, *Escherichia coli* isolates in girls were significantly more sensitive ($p < 0.0001$) to ampicillin (41% vs. 30%) and amoxicillin/clavulanic acid (82% vs. 72%) than in boys.
Conclusions: The compilation of cumulative susceptibility reports disaggregated by age or gender reveals significant differences. In our setting, cefuroxime may be considered the first-line empirical treatment in pediatric patients.

Sensibilidad antimicrobiana de microorganismos causantes de infecciones del tracto urinario en pacientes pediátricos

Palabras clave:
Sensibilidad antimicrobiana
Pediatría
Infección del tracto urinario
Informes de sensibilidad acumulada
Epidemiología

RESUMEN

Introducción: Los informes de sensibilidad acumulada son una herramienta valiosa para guiar el tratamiento empírico de infecciones urinarias, sobre todo en el contexto actual de crecientes tasas de resistencia. Nuestro objetivo es analizar la sensibilidad antimicrobiana de bacterias aisladas de urocultivos de pacientes pediátricos durante un período de 5 años.
Métodos: Estudio retrospectivo de los urocultivos del período 2011-2015. La identificación y estudios de sensibilidad se realizaron con el sistema Vitek-2 (BioMérieux®) y se interpretaron según los criterios

* Corresponding author.
E-mail address: jrguezlozano@gmail.com (J. Rodríguez-Lozano).

de EUCAST. Se analizaron los datos de sensibilidad antimicrobiana según sexo y tramos de edad (neonatos, 1 mes-5 años, 5-15 años) y se compararon con los datos de mayores de 15 años.
Resultados: En el período analizado se procesaron 17.164 urocultivos de 7.924 pacientes menores de 16 años. Los porcentajes de sensibilidad en estos pacientes fueron: ampicilina 36,3%; amoxicilina/clavulánico 75,3%; cefuroxima 83,2%; cotrimoxazol 68,9%; ciprofloxacino 85,3%; fosfomicina 85,5%; nitrofurantoína 84,4%, y cefalosporinas de tercera generación 89-91%. Aminoglucósidos (>92%) y carbapenemas (95%) mantienen las mayores tasas de sensibilidad. La prevalencia de aislamientos productores de BLEE fue significativamente menor en niños menores de 16 años (1,5% vs. 4,1%). En menores de 16 años, los aislamientos de *Escherichia coli* procedentes de mujeres fueron significativamente ($p < 0,0001$) más sensibles a ampicilina (41% vs. 30%) y amoxicilina-clavulánico (82% vs. 72%) que en varones.
Conclusiones: La elaboración de informes de sensibilidad acumulados desglosados por edad o sexo permite detectar importantes diferencias. En nuestra área, cefuroxima puede considerarse como primera opción de tratamiento empírico en pacientes pediátricos.

Introduction

Urinary tract infection (UTI) is the second most common infection in pediatric patients, with *Escherichia coli* being its first cause. Because of the possible complications that may lead to long-term hospital stay and, especially in children, to renal scarring, hypertension or chronic kidney disease,[1,2] often require physicians to prescribe empirical antimicrobial therapy. This leads to growing consumption of antibiotics increasing selective pressure and favoring antimicrobial resistance. Current guidelines establish that uncomplicated UTIs in children should be treated empirically with short-course oral antimicrobials.[2,3] But, in recent years, increasing resistance to antimicrobial agents has been reported worldwide. In this context, cumulative reports on antimicrobial susceptibility data provided by microbiological laboratories are important for selecting empirical treatments. This is of particular relevance in case of UTI.[4] However, there is a paucity of such data related to pediatrics patients.

The aim of this study is to retrospectively analyze antimicrobial susceptibility data of microorganism isolated from pediatrics patients in our healthcare area during the last years and to compare them with those obtained from adult patients.

Materials and methods

A retrospective observational study of urine cultures analyzed in the period of January 2011to December 2015 at the Microbiology Service of the University Hospital Marqués de Valdecilla (Santander, Northern Spain) was conducted. Our institution covers a healthcare area of 330 000 inhabitants (44 800 children under the age of 15 years).

All urine samples were inoculated on Cysteine lactose electrolyte deficient agar plates (CLED, Oxoid™, Wesel, Germany) with a 0.001 mL calibrated loop. In case of immunosuppressed patients or urine samples obtained by suprapubic bladder aspiration or catheterism, sheep blood agar plates were also inoculated. Colony counts $>10^4$ (or 10^2 in case of suprapubic bladder aspiration and 10^3 in case of catheterism) were considered positive. Isolation of more than 2 microorganisms was considered an indication of a contaminated urine sample.

Identification and susceptibility testing has been performed with GP-ID, GN-ID, AST-626, AST-589 and AST-244 cards (Vitek-2, bioMérieux, L'Étoile, France). Ampicillin, amoxicillin plus clavulanate, cefuroxime, cefoxitin, cefotaxime, ceftazidime, cefepime, imipenem, ertapenem, amikacin, gentamicin, tobramycin, nalidixic, ciprofloxacin, trimethoprim-sulfamethoxazole, fosfomycin and nitrofurantoin were studied. Categorical interpretation of susceptibility data was defined following EUCAST breakpoints,[5] except for amoxicillin-clavulanic acid (ratio 2:1 in the Vitek cards we used, which was interpreted according to CLSI breakpoints.[6] Ciprofloxacin-susceptible enterobacteria with a MIC of nalidixic acid >16 mg/L (indicating low-level quinolone resistance) was reported as ciprofloxacin intermediate in our laboratory.

Antimicrobial susceptibility data (first isolate of each microorganism per patient and year) was stratified by gender and age of the patient, and classified into three pediatric groups (neonates, 1 month to 5 years and 5–15 years). These data was compared with that obtained from patients older than 15 years. We analyzed susceptibility data of all microorganisms grouped together and for each microorganismseparately. Not all antimicrobial agents analyzed were tested for all microorganisms, due to the different designs of Vitek-2 cards we used. To avoid bias in the overall analysis of all microorganisms grouped; we deducted the susceptibility of antimicrobials not tested considering microorganism identification and other antimicrobial susceptibility results. For example, amoxicillin–clavulanate, ertapenem and imipenem were interpreted as susceptible in case of ampicillin-susceptible enterococci; cephalosporins and aminoglycosides were considered as resistant in enterococci; ampicillin, amoxicillin plus clavulanate, cefuroxime, cefoxitin and cefotaxime were interpreted as resistant in *Pseudomonas* spp., etc.[7,8]

The presence of ESBL producing microorganisms was analyzed and compared between the different pediatric age groups. ESBL-producing strains were characterized by PCR targeting TEM, SHV and CTX-M gene families and by sequencing of the obtained amplicons.[9–11]

Comparative analysis of antimicrobial susceptibility results was determined using χ^2, and when it was not suitable, a Fisher's exact test was used.[4] A p value of ≤ 0.05 was considered statistically significant.

Results

Duringthe study period 17 164 urine samples from 7924 patients younger than 16 years were processed, they came from primary care (55.1%), hospitalized patients (6.5%), outpatient visits (21.8%), and emergency departments (16.6%). Urine culture was defined as positive in 3751 samples (21.8%) and *E. coli* was the most frequently isolated uropathogen (2370 patients, 63.2%), followed by *Proteus mirabilis* (374 patients, 10%), *Klebsiella pneumoniae* (189 patients, 5%), *Klebsiella oxytoca* (148 patients, 3.9%), *Enterococcus faecalis* (138 patients, 3.7%), *Pseudomonas aeruginosa* (118 patients, 3.1%) and *Enterobacter cloacae* complex (81 patients, 2.2%) (Table 1).