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ORIGINAL ARTICLE

Drug susceptibility and treatment response of common urinary tract infection pathogens in children

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Background/Purpose: To document the trends of sensitivity and to find whether it is necessary to change antibiotics in selected patients according to the sensitivity test results in our clinical practice.
Methods: We collected urine culture results from 0–18-year-old patients in the National Taiwan University Hospital from January 1, 2003 to October 31, 2012. Their medical chart was reviewed to identify true pathogens responsible for their urinary tract infection (UTI). We checked the percentage of susceptibility of these pathogens to ampicillin, amoxicillin–clavulanate (AMC), cefazolin, cefmetazole, ceftriaxone, gentamicin, and trimethoprim–sulfamethoxazole (TMP–SMX) according to the Clinical and Laboratory Standards Institute (CLSI) guideline. The extended-spectrum-beta-lactamases (ESBLs) rate was also checked. In addition, we reviewed the treatment response of different antibiotics. Defervescence within 48 hours after initial antibiotics use was considered responsive.
Results: A total of 7758 urine cultures positive for *Escherichia coli* infection were collected during the 10-year period. The *E. coli* cefazolin susceptibility rate was 62–73% during 2003–2010, but it dropped to 23% in 2011 and 28% in 2012 after the new CLSI guideline (M100-S21) was released. However, other antibiotics did not show a significant difference. In UTI caused by *E. coli*, on average, the sensitivity rates for various antibiotics were as follows:

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cefmetazole, 90%; ceftriaxone, 85%; gentamicin, 77%; AMC, 61%; TMP−SMX, 47%; and ampicillin, 20%. The ESBL rate was also found to increase (2−11%; $p < 0.01$). The overall response rate of UTI caused by *E. coli* to first-line antibiotics such as first-generation cephalosporin and/or gentamicin was 78%.

Conclusion: The susceptibility of common urinary tract pathogens to cefazolin has decreased dramatically since 2010. This trend may be due to the change in the CLSI guideline. Although the susceptibility rate to first-line empirical antibiotics shows a decreasing trend, we found that the clinical response was acceptable for our first-line empirical antibiotics.

Introduction

Urinary tract infection (UTI) is a common disease in children and usually causes hospitalization. We found that the common pathogens of UTI (*Escherichia coli*, *Klebsiella pneumoniae*, and *Proteus* spp.) had increasing resistance to our empirical antibiotics.

In most hospitals, the drug susceptibility is usually tested according to the Clinical and Laboratory Standards Institute (CLSI) guideline. However, the cefazolin and ceftriaxone breakpoints have been revised in the CLSI guideline released in 2010 and 2011.[1−3] In our microbiological laboratory setting, we used zone diameter as breakpoints to interpret drug sensitivity. Prior to 2010, the zone diameter cutoff point for cefazolin to test isolates of Enterobacteriaceae was ≥18 mm (sensitive), 15−17 mm (intermediate), and ≤14 mm (resistance); for ceftriaxone, it was ≥21 mm (sensitive), 14−20 mm (intermediate), and ≤13 mm (resistance).[1] However, in the new CLSI standard, the cutoff point for cefazolin is ≥23 mm (sensitive), 20−22 mm (intermediate), and ≤19 mm (resistance).[2] For ceftriaxone, it is ≥23 mm (sensitive), 20−22 mm (intermediate), and ≤19 mm (resistance). The minimum inhibitory concentration (MIC) or zone diameter breakpoints of other commonly used antibiotics such as ampicillin, amoxicillin−clavulanate (AMC), cefmetazole, gentamicin, and trimethoprim−sulfamethoxazole (TMP−SMX) were not changed in the new CLSI guideline.

In our clinical practice, it is crucial to choose a suitable antibiotic for the treatment of UTI. In the new CLSI guideline (M100-S21) era,[2] it seems that the common UTI pathogens have high resistance to the empirical antibiotics such as the first-generation cephalosporin. We wondered whether changing antibiotics according to the sensitivity test results is necessary in specific patients. The aim of this study was to investigate the trends of antibiotic sensitivity and evaluate the clinical response of different antibiotics in children with UTIs.

Methods

Patient collection

We collected the urine culture results from 0−18-year-old patients in the National Taiwan University Hospital from January 1, 2003 to October 31, 2012. Patient's medical chart was reviewed to identify true UTI pathogens. True UTI pathogen was defined as a single pathogen with adequate colony formation unit (CFU) in one urine culture specimen according to the sampling methods (i.e., >100,000 CFU/mL in voiding urine; >10,000 CFU/mL in catheterized urine; and >1000 CFU/mL in suprapubic puncture).[4]

Drug susceptibility test

In vitro susceptibility was determined by the broth microdilution method and susceptibility profiles were determined based on the CLSI guideline.[1−3] We used zone diameter as breakpoints to measure drug sensitivity. The MIC interpretive standard for cefazolin to test isolates of Enterobacteriaceae was ≤8 μg/mL (sensitive), 16 μg/mL (intermediate), and ≥32 016 μg/mL (resistance) prior to 2010, and these were revised to ≤2 μg/mL (sensitive), 4 μg/mL (intermediate), and ≥8 μg/mL (resistance) after 2010. For ceftriaxone, the MIC interpretive standard was ≤8 μg/mL (sensitive), 16−32 μg/mL (intermediate), and ≥64 μg/mL (resistance) prior to 2010, and these were revised to ≤1 μg/mL (sensitive), 2 μg/mL (intermediate), and ≥4 μg/mL (resistance) after 2010.[1−3] The MIC or zone diameter breakpoints of other commonly used antibiotics such as ampicillin, AMC, cefmetazole, gentamicin, and TMP−SMX were not changed in the new CLSI guideline.

Extended-spectrum-beta-lactamases (ESBLs) testing is accomplished by a double-disk synergy test according to the CLSI guideline.[1−3] A greater than 5-mm increase in a zone diameter for either antimicrobial agent tested in combination with clavulanic acid versus the zone diameter of the agent when tested alone is defined as ESBL-producing strains (i.e., a ceftazidime−clavulanic acid zone 5 mm bigger than a ceftazidime zone is called ESBL-producing strains). Carbapenemase-producing isolates are tested according to the disk diffusion method based on the CLSI guideline. Intermediate or resistant to one or more carbapenems is defined as carbapenem resistance (CR). We used ertapenem nonsusceptibility, which is the most sensitive indicator of carbapenemase production, as the standard of defining CR.

Clinical data collection

E. coli, *K. pneumoniae*, *Proteus* spp., and *Enterococcus* spp. are the most common pathogens responsible for causing UTI in children. Those people who had a positive