Antibiotic Susceptibility of Common Pediatric Uropathogens in the United States

TO THE EDITOR—Urinary tract infections (UTIs) remain a common indication for antibiotic therapy in children [1]. They are frequently managed in the outpatient setting where availability of susceptibility results may be delayed, making selection of appropriate initial therapy important. We sought to evaluate susceptibility patterns of antibiotic agents used to treat UTIs in children by developing a pooled antibiogram of urinary isolates from pediatric hospitals across the United States.

We obtained 2012 and 2013 antibiotic susceptibility data for pediatric urinary isolates using methods previously described [2]. Susceptibility data were collected separately for institutions that have and have not incorporated the Clinical and Laboratory Standards Institute (CLSI) recommendations to lower cefazolin breakpoints from ≤8 µg/mL to ≤2 µg/mL against Enterobacteriaceae [3]. Comparisons were made using χ² analysis.

Data were obtained from 43 hospitals (Table 1). The addition of clavulanate to amoxicillin increased activity against Escherichia coli, the most common uropathogen isolated, from 49% to 75%. Ceftriaxone had the highest activity against E. coli at 97%. Cefazolin was active against 90% of E. coli isolates using a breakpoint of 8 µg/mL and 47% of isolates for institutions using a breakpoint of 2 µg/mL (P < .001). Cephalothin, another first-generation cephalosporin, had activity against 56% of E. coli isolates.

Third-generation cephalosporins continue to have excellent activity against common gram-negative pediatric uropathogens, but because they can accelerate the development of extended-spectrum β-lactamases [4], other, narrower-spectrum agents should be considered whenever possible. Approximately 90% of E. coli are susceptible to cefazolin (or cephalexin) when a breakpoint of 8 µg/mL is used, decreasing to <50% with a breakpoint of 2 µg/mL. The cefazolin breakpoint changes were mainly influenced by adult pharmacokinetic/pharmacodynamic simulation studies, without special consideration for urinary isolates [3]. In the absence of clinical data to support the revised cefazolin breakpoints, our findings underscore the need to reexamine their rationale.

Cephalothin activity is currently used as a proxy for susceptibility to other cephalosporins by 21% of hospitals, although recently discouraged by the CLSI [5]. Our results suggest that cephalothin is not a reliable predictor of cephalexin susceptibility. This is important as institutions may consider cephalexin a suboptimal choice based on cephalothin results and resort to prescribing increasingly broad-spectrum antibiotics [5].

Widespread amoxicillin resistance in E. coli, with minimal improvement with the addition of clavulanate, undermines its effectiveness as an empiric agent. Similarly, caution should be used when trimethoprim-sulfamethoxazole is prescribed on an empiric basis as it has activity against 68% of E. coli isolates. Although nitrofurantoin has activity against 95% of E. coli isolates, its poor renal parenchymal penetration precludes its use for pyelonephritis [1].

We were unable to separate urinary isolates obtained from relatively healthy...
children from those with frequent healthcare exposure, possibly underestimating susceptibility results for the former and overestimating susceptibility results for the latter. Antibiotic susceptibility results from bacteria isolated in prior urine cultures should always supersede an antibiogram when selecting empiric UTI therapy. Our pooled antibiogram is useful for hospitals without sufficient pediatric urinary isolates or laboratory resources to generate institutional pediatric urinary antibiograms. As first-generation cephaplorins are known to concentrate well in the urine and clinical outcomes data do not suggest worse outcomes for patients with E. coli UTIs treated with cephalaxin with minimum inhibitory concentrations of 2–8 µg/mL compared with 1 µg/mL, the benefit of the lowered breakpoints should be revisited.

Notes
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Table 1. Pooled Proportions of Antibiotic Susceptibility Data for Uropathogens From 43 Participating Pediatric Institutions Across the United States, 2012–2013

<table>
<thead>
<tr>
<th>Organism</th>
<th>No. of Isolates Tested</th>
<th>Amoxicillin</th>
<th>Amoxicillin clavulanate</th>
<th>Cefazolin (Susceptible ≤8 µg/mL)</th>
<th>Cefazolin (Susceptible ≤2 µg/mL)</th>
<th>Cephalothin</th>
<th>Ceftriaxone</th>
<th>Ciprofloxacin</th>
<th>Nitrofurantoin</th>
<th>TMP-SMX</th>
</tr>
</thead>
<tbody>
<tr>
<td>Enterococcus faecalis</td>
<td>3220</td>
<td>99</td>
<td>3221</td>
<td>98</td>
<td>3221</td>
<td>98</td>
<td>3221</td>
<td>98</td>
<td>3221</td>
<td>98</td>
</tr>
<tr>
<td>Escherichia coli</td>
<td>41,539</td>
<td>49</td>
<td>30,886</td>
<td>75</td>
<td>20,029</td>
<td>90</td>
<td>10,934</td>
<td>47</td>
<td>16,625</td>
<td>56</td>
</tr>
<tr>
<td>Klebsiella pneumoniae</td>
<td>2913</td>
<td>0</td>
<td>3950</td>
<td>88</td>
<td>2637</td>
<td>93</td>
<td>865</td>
<td>75</td>
<td>1357</td>
<td>89</td>
</tr>
<tr>
<td>Proteus mirabilis</td>
<td>3524</td>
<td>83</td>
<td>2,572</td>
<td>95</td>
<td>1,680</td>
<td>91</td>
<td>881</td>
<td>50</td>
<td>1,208</td>
<td>93</td>
</tr>
<tr>
<td>Pseudomonas aeruginosa</td>
<td>3,342</td>
<td>90</td>
<td></td>
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Abbreviation: TMP-SMX, trimethoprim-sulfamethoxazole.

a Cefazolin breakpoints of 8 µg/mL and 2 µg/mL were used by 76% and 24% of included institutions, respectively.


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