Fosfomycin Susceptibilities Among Uropathogenic
Extended Spectrum Beta-Lactamase-producing Enterobacteraeae

Lilian M Abbo, M.D.1, Aida E Casiano-Colon, PhD.2, Marissa Tysiak, Pharm.D.3, Thomas M. Hooton, M.D.1
1University of Miami Miller School of Medicine, Department of Medicine, Division of Infectious Diseases; 2Integrated Regional Laboratories, Ft. Lauderdale, Florida; 3University of Miami Hospital Department of Pharmacy, Miami, Florida.

Background:

• Antimicrobial resistance among uropathogens is a global problem with limited therapeutic alternatives.
• The Urinary Tract Infection Drug Resistance Index (UTI-DRI) in the South-Atlantic Region of the United States has steadily increased in the last decade by 60% (baseline 16.9 in 1999 to 27.1 in 2010)1.
• Fosfomycin is a broad-spectrum antimicrobial that has attracted interest for the treatment of lower UTIs caused by Gram-negative uropathogens resistant to extended-spectrum beta lactams (ESBLs)2.
• Data regarding antimicrobial susceptibilities for Enterobacteriaceae in the US, especially for fosfomycin, are scarce. Of concern, there are reports that suggest resistance to fosfomycin may be increasing in Europe, where the drug is used widely3.

Methods:

• Retrospective review of urine cultures performed at Integrated Regional Laboratories (IRL) serving 14 acute care (ACF) and 5 long-term care facilities (LTCF) in South Florida between January 2013 and August 2014.

• Urine cultures were from hospitalized patients, emergency departments and residents in LTCF. Only Enterobacteriaceae isolates that tested non-susceptible to extended spectrum beta-lactam (ESBL) were included in the analysis.
• Isolates were considered to be ESBL-producing if they were intermediate (I), susceptible dose dependent (SDD), or resistant (R) to any 3rd or 4th generation cephalosporin per the 2014 Clinical Laboratory Standards Institute (CLSI) breakpoints. Fosfomycin Kirby-Bauer disk diffusion susceptibilities were determined using a 200 ug disk.
• 2014 CLSI breakpoints for gram negative organisms were used to interpret fosfomycin results for E.coli and other “non-E. coli” isolates in urine

<12mm Resistant; 13-15mm Intermediate; >=16mm Susceptible
Equivalent MIC Interpretative Criteria: <64ug/ml S; 128ug/ml I; >256ug/ml R

Results:

• ESBL-producing Enterobacteriaceae strains from 1463 ACF and 411 LTCF urine cultures were analyzed.
• The number of E. coli isolates ranged from 16-170 in ACF and 4-136 in LTCF.
• More cultures were tested in 2014 than in 2013. Susceptibilities for each organism were similar by year at both ACF (Table 1) and LTCF (Table 2) except for K. pneumoniae strains which were less susceptible in 2014.
• For E.coli 97% of isolates in ACF and 95% in LTCF in 2014 were susceptible.

Table 1. Number and percent of urinary isolates susceptible to fosfomycin in Acute Care Facilities (ACFs)

<table>
<thead>
<tr>
<th>Species</th>
<th>2013</th>
<th>2014</th>
</tr>
</thead>
<tbody>
<tr>
<td>E. coli</td>
<td>214/224 (96%)</td>
<td>891/920 (97%)</td>
</tr>
<tr>
<td>K. pneumoniae</td>
<td>60/70 (86%)</td>
<td>148/194 (76%)</td>
</tr>
<tr>
<td>K. oxytoca</td>
<td>4/4 (100%)</td>
<td>18/18 (100%)</td>
</tr>
<tr>
<td>P. mirabilis</td>
<td>5/7 (71%)</td>
<td>19/26 (73%)</td>
</tr>
</tbody>
</table>

All | 383/305 (93%) | 1076/1158 (93%) |

Table 2. Number and percent of urinary isolates susceptible to fosfomycin in Long Term Care Facilities (LTCFs)

<table>
<thead>
<tr>
<th>Species</th>
<th>2013</th>
<th>2014</th>
</tr>
</thead>
<tbody>
<tr>
<td>E. coli</td>
<td>78/79 (99%)</td>
<td>244/233 (95%)</td>
</tr>
<tr>
<td>K. pneumoniae</td>
<td>9/10 (90%)</td>
<td>52/65 (80%)</td>
</tr>
<tr>
<td>K. oxytoca</td>
<td>No data</td>
<td>4/4 (100%)</td>
</tr>
<tr>
<td>P. mirabilis</td>
<td>No data</td>
<td>9/9 (100%)</td>
</tr>
</tbody>
</table>

All | 87/89 (98%) | 298/322 (93%) |

Conclusions:

• Microbiology laboratories in the US often do not perform antimicrobial susceptibility testing against fosfomycin, so that clinicians treating cystitis caused by known or presumptive ESBL-producing strains must do so empirically.
• Our data show that fosfomycin has excellent in vitro activity against urinary ESBL-producing Enterobacteriaceae strains, especially E. coli, in South Florida ACFs and LTCFs.
• We do not have demographic data on patients from whom these isolates were grown, but it seems likely that isolates from young and old ambulatory women with cystitis would likely have a similar susceptibility profile.
• Fosfomycin, along with nitrofurantoin, is a first-line alternative for the treatment of acute uncomplicated cystitis – these data support this recommendation in South Florida.

References:

drug_resistance_index_ureteric_tract_and_skin_infections
3. Rodríguez-Avil C, Rodríguez-Avil I, Hernández E, Picazo JJ. Increasing prevalence of fosfomycin-resistant ESBL-producing Enterobacteriaceae from young and old ambulatory women with cystitis would likely have a similar susceptibility profile. Our data show that fosfomycin has excellent in vitro activity against urinary ESBL-producing Enterobacteriaceae strains, especially E. coli, in South Florida ACFs and LTCFs.