Resistance to Oral Antibiotics among Urinary Tract Infection Isolates of *Escherichia coli* from the United States and Europe in 2017

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**INTRODUCTION**

*Escherichia coli* is the most prevalent pathogen associated with urinary tract infections (UTIs). Oral antibiotics including the cephalosporins, fluoroquinolones and trimethoprim sulfamethoxazole (TMP-SMX) have been historically used to manage UTIs but in recent years their utility has been eroded by the increasing prevalence of extended spectrum β-lactamase (ESBL)-producing organisms whose resistance co-effect has been reported. The management of UTIs caused by ESBL-producing *E. coli* is challenging due to limited oral treatment options being available outside the hospital setting. The carbapenem antibiotics are one of the few classes that have retained activity because of their stability to ESBL and Class C β-lactamases that are prevalent among Gram-negative uropathogens. Unfortunately, no oral options with the spectrum and potency of the carbapenems are currently available. The goal of the current study was to assess the susceptibility of UTI isolates of *E. coli* collected in the United States and Europe during 2017 to various antibiotics, including oral agents widely used to treat UTIs to assess rates of resistance in both continents. The prevalence of ESBL phenotypes among *E. coli* will also be assessed to determine the impact of co-resistance to oral antibiotics.

**METHODS**

*E. coli* from UTIs were collected as part of the SENTRY Surveillance Program (JMI Laboratories, North Liberty, IA) from participating medical centers geographically distributed across the nine US Census regions and from 11 countries in Europe. All isolates were centrally tested for susceptibility and the results were interpreted in accordance with CLSI and EUCAST criteria. All ESBL phenotypes were defined by CLSI criteria and were used to select isolates for follow up molecular characterization to confirm the presence of specific β-lactamase genes such as the CTX-M-15 ESBL. Molecular analyses were conducted using next generation sequencing (NGS). Susceptibility results for all UTI isolates including ESBL phenotypes, FO-resistant, TMP-SMX-resistant phenotypes and CTX-M-15 genotypes were determined using the publicly available SENTRY Antimicrobial Surveillance online query tool (1).

**RESULTS**

**Table 1:** Susceptibility Results for 2,422 UTI isolates of *E. coli* collected in the US and EU in 2017 in the SENTRY Surveillance program.

**Table 2:** Co-resistance among TMP-SMX-R and levofloxacin-R *E. coli* from UTIs in US and EU during 2017.

**Table 3:** Susceptibility Results for 167 CTX-M-15 β-lactamase-positive *E. coli* from UTIs in the US and EU during 2017.

**CONCLUSIONS**

- Among the 2,422 UTI isolates of *E. coli* resistance to FGs were 28.1% and 27.4%, respectively, for ciprofloxacin and levofloxacin. Using oral breakpoints 38.6% of *E. coli* were non-susceptible to cefuroxime and 33.2% of isolates were resistant to TMP-SMX (Table 1). 16.5% (460 isolates) were R to both levofloxacin and TMP-SMX.
- Overall prevalence of ESBL phenotypes among *E. coli* was 18.2% (18.7% in the US and 21.5% in the EU).
- Among the 411 ESBL phenotypes, R to cefuroxime, levofloxacin and TMP-SMX were 94.3%, 70.8% and 61.6%, respectively. Resistance to oral antibiotics were similar, regardless of continent (Figure 1) but trended slightly higher for isolates from the EU compared with US. Intravenous carbapenems were highly active against ESBL isolates of *E. coli* from both the US and EU. Only two carbapenem-resistant *E. coli* were identified in the EU; an NDM-5 β-lactamase-encoding organism from Turkey and a KPC-2 producing organism from Greece.
- Levofloxacin-resistant *E. coli* exhibited high co-resistance to cefuroxime (49.5%) and TMP-SMX (52.2%). TMP-SMX R *E. coli* exhibited high co-resistance to FGs such as levofloxacin (48.8%), and cefuroxime (34.3%). In contrast, all levofloxacin-R and TMP-SMX-R *E. coli* exhibited low or no co-resistance to the carbapenems (Table 23).
- CTX-M-15 ESBL genotypes were the most prevalent ESBL's and were identified among 167 *E. coli*. Among the CTX-M-15 genotypes FG-R was 85.6% for levofloxacin and R to TMP-SMX was 70.7% (Table 3).
- The carbapenems retained activity with high susceptibility rates against UTI isolates of *E. coli* from both the US and EU including resistant phenotypes and confirmed genotypes.
- New oral agents with the spectrum and potency of the intravenous carbapenems would address a substantial unmet need for new agents to treat UTIs caused by multi-drug-resistant ESBL-producing *E. coli*.

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1. Ian A. Critchley, Dr. F. David, N. Cotroneo, K. A. Sulham, D. Melnick, R. Mendes. Resistance to Oral Antibiotics among Urinary Tract Infection Isolates of *Escherichia coli* from the United States and Europe in 2017. *Spero Therapeutics* 675 Massachusetts Ave 14th Floor Cambridge, MA 02139 Phone: (303) 564-5139 E-mail: icritchley@sperotherapeutics.com