Disclosures. H. S. Sader, Allergan: Research Contractor, Research support. M. Castanheira, Allergan: Research Contractor, Research support. R. E. Mendes, Allergan: Research Contractor, Research support. R. K. Flamm, Allergan: Research Contractor, Research support.

1524. Are Providers Shifting from NTF to Fosfomycin for Inpatient UTI? Big Data Reveals Small Shifts Kalpana Gupta, PhD MPH1; Matthew B. Goetz, MD1; Makoto Jones, MD, MS1; and Judith M. Smyth, MD1; 1VA Boston Healthcare System, West Roxbury, MA; 2Boston University School of Medicine, Boston, Massachusetts; 3David Gelfen School of Medicine, University of California, Los Angeles, Los Angeles, California

Methods. This retrospective study included patients who received fosfomycin for the treatment of a UTI caused by any Enterobacteriaceae for which fosfomycin testing was performed from March 2016 through April 2018. We separated patients who received fosfomycin for the treatment of UTIs caused by E. coli from those caused by other Enterobacteriaceae for comparison. The primary outcome is the rate of clinical success at 48 hours, defined as the absence of UTI symptoms and normalization of vital signs. The secondary outcome is the rate of recurrent UTIs caused by the same pathogen within 30 days of the index infection.

Results. There were 28 separate episodes of E. coli UTIs in 24 patients and 25 separate episodes of non-E. coli UTIs in 26 patients included in this study. Patients were mostly balanced between the two groups and were on average about 64 years old, mostly females (61%), and had an average Charlson Comorbidity Index of 5. All E. coli isolates were susceptible to fosfomycin, while only 82.8% of non-E. coli isolates were fosfomycin-susceptible. The rates of clinical success were similar between the E. coli and non-E. coli groups (89.3% vs. 88.5%). There was a higher rate of recurrence of the same UTI with E. coli (15.4%) than with non-E. coli (4.8%).

Conclusion. Findings from this small study suggest favorable outcomes with use of fosfomycin for non-E. coli Enterobacteriaceae. Despite recommendations against testing and use of fosfomycin in these pathogen groups, it appears that in vitro resistance does not always correlate with clinical response.

Disclosures. All authors: No reported disclosures.

1526. Oral Fosfomycin Use for Urinary Tract Infections and Its Clinical Impact on Hospital Stay

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Methods. This retrospective study included patients who received fosfomycin for UTI caused by multi-drug resistant organisms (MDRO). The objective of the study was to describe the prescribing pattern of fosfomycin and determine its role in (1) preventing hospital admissions for patients seen in the emergency department or (2) promoting earlier discharges for admitted patients.

Results. Forty-three patients were included (60.5% females). Nearly half of the population (48.8%) had a history of recurrent UTIs. Patients received fosfomycin for cystitis (58.1%), pyelonephritis (34.9%), and asymptomatic bacteriuria (7%). Only two patients received >1 dose. Empiric use of fosfomycin was seen in only 9.3%. Of those treated based on culture results, 84.6% of patients had MDROs (2 ESBL, 2 VRE, 1 KPC, 1 resistant-Pseudomonas). No isolates had fosfomycin susceptibilities performed. In 72% of the time, patients had no other oral options. In 74.3% of the time, fosfomycin was used as step-down therapy from intravenous (IV) antibiotics (e.g., carbapenems 69%, ceftazidime 13.8%). Infectious Diseases was consulted on 81.4% of cases. Seven percent of patients had demonstrated allergies to the preferred agent. Treatment success was seen in 93% of patients, while three patients failed treatment requiring readmission for IV therapy. Fosfomycin use resulted in earlier discharge in 75.8% of cases (range of 1–6 days, mean 2.92 hospital days avoided per patient). For those who received fosfomycin as part of their emergency visit, 90% (9 of 10) were able to avoid hospitalization.

Conclusion. In our study, fosfomycin was used in UTI caused by MDROs, with treatment success demonstrated in a majority of patients. Fosfomycin allowed for patients to avoid hospitalization or promote earlier discharge, on average treated for days sooner than anticipated. Use of fosfomycin should be considered in appropriate patients in an effort to decrease length-of-stay or altogether avoid hospitalization.

Disclosures. All authors: No reported disclosures.

1527. The Prevalence of Enterobacteriaceae (ENT) Resistant to All Major Classes of Oral Antibiotics from Outpatient Urine Cultures in the United States and Effect of Clinical Outcomes

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Methods. This was a prospective, national study. A total of 10,000 outpatient urine cultures from a random sample of retail pharmacies in the United States was collected from November 2016 to September 2018. The isolates included were: Escherichia coli, Enterococcus faecalis, and Escherichia coli. The prevalence of Enterobacteriaceae (ENT) resistant to all major classes of oral antibiotics from outpatient urine cultures in the United States and effect of clinical outcomes is described.

Results. Of 10,000 urine cultures, 7,999 were positive for ENT and 99% were included in the analysis. The ENT most commonly isolated was E. coli (95.3%). The prevalence of ENT resistant to all major classes of oral antibiotics was 41.5% overall and varied by geographic region. The highest prevalence was in the Midwest (46.5%) and the lowest was in the South (36.7%). The prevalence of ENT resistant to all major classes of oral antibiotics was significantly higher in patients with a history of recurrent ENT (48.1%) compared to those without a history of recurrent ENT (39.4%). The prevalence of ENT resistant to all major classes of oral antibiotics was significantly higher in patients with a history of recurrent ENT who were treated with a quinolone, β-lactam, trimethoprim-sulfamethoxazole (T/S) or nitrofurantoin (NFH) compared to those who were treated with other antibiotics (46.8% vs. 40.5%). Resistance to all classes of antibiotics is now

Disclosures. All authors: No reported disclosures.

References

1. Fosfomycin (FOS) and NTF (NTF) are IDSA guideline approved drugs for acute cystitis in women. However, their activity against multi drug-resistant Gram-negatives may be driving increased use among inpatients with more complicated UTI. We evaluated trends in inpatient prescribing of these UTI-specific agents in the predominantly male population of the national VA system over a 7-year period.

Methods. All inpatient bar coded administrations for FOS and NTF at every VA facility nationwide from 2011 to 2017 were captured through a data analytics platform which extracts data from the VA Data warehouse. Antibiotic days of therapy and rates per 1,000 patient-days (DOT/1,000CD) were extracted by year and compared using Mantel-Haenszel chi square for linear trend (MH OR). Demographics were captured via administrative data.

Results. Prescriptions from over 65 million patient-days spanning 7 years and all inpatient units in 129 VA facilities were included. Approximately 90% of patients were male with a mean age range of 55–64 years. FOS use increased from 128 prescriptions in 2011 to a high of 1,230 in 2016 and 1,003 in 2017 (figure). At the maximum in 2016, prescription rates increased almost 10-fold compared with 2011 (MH OR 9.8, P < 0.001). NTF prescriptions declined from 26,590 in 2011 to 19,343 in 2017. Rates decreased 25% from 2.8 to 2.1, MH OR 0.75, P < 0.001. In 2017, FOS and NTF usage rates were highest in rehabilitation/spinal cord units (table).

Conclusion. In this large nationwide cohort, FOS use increased almost 10-fold among predominantly male inpatients while NTF use declined slightly. NTF is still used orders of magnitude more than FOS, even after adjusting for extended days of therapy and rates per 1,000 patient-days (DOT/1,000CD) were extracted by year and compared using Mantel-Haenszel chi square for linear trend (MH OR). Demographics were captured via administrative data.

References

1. National Trends in Inpatient Fosfomycin and Nitrofurantoin Usage

| Year | DOT/1,000CD | ICU | MDSURG | NH | PSYCH | REHAB/SCI |
|------|-------------|-----|--------|----|-------|-----------|
| 2017 | 0.06        | 0.15 | 0.07   | 0.03 | 0.73  |
| 2018 | 0.56        | 1.46 | 2.41   | 2.55 | 9.35  |
| 2019 | 0.58        | 3.39 | 2.99   | 2.63 | 4.03  |

Disclosures. All authors: No reported disclosures.
reported in the US, making the selection of empiric oral therapy increasingly unlikely to cover the offending uropathogen.

Methods. We queried the BD Insights Research Database (Franklin Lakes, NJ) to evaluate ambulatory antibiotic pill history for patients from 15 US institutions with an ambulatory urine culture positive for ≥10^5 CFU/mL of an ENT. Patients who filled a prescription for an oral antibiotic were further categorized into those with a urine culture positive for a susceptible or non-susceptible (NS) pathogen. ESBL positivity was presumed if the isolate was NS to extended spectrum cephalosporins. Outcome was assessed using two surrogate endpoints: hospital admission, or a follow-up oral antibiotic within 28 days of initial antibiotic fill. Urine 30 day nonduplicate ambulatory three drug resistance rates in Q2 2017 were determined by zip code for 379 facilities.

Results. 48/5,587 (0.9%) episodes of UTI with an outpatient urine culture had an Enterobacteriaceae that was resistant to quinolones, T/S, and NFH, and was ESBL-positive. Of those with at least three drug-resistance classes, the hospital admission rate was 28%.

|            | 28-Day Prescription Filled | 28-Day Readmission |
|------------|-----------------------------|--------------------|
|            | N (%)                        | Fail % P-Value     |
| Overall    | 5,587                        | 1250 22            |
| Pan-susceptible | 1,771            | 297 16 0.0001      |
| 3-4 Class Resistance | 197 (4)        | 55 28            |

*All resistant to quinolones, T/S, and β-lactams; four class also includes resistance to NFH.

Figure. Geographic prevalence of three drug class resistance (quinolones, β-lactam, T/S) among Enterobacteriaceae causing UTI in the outpatient setting.

Conclusion. Multidrug resistance to existing oral antibiotics is prevalent throughout the United States in patients for whom an outpatient urine culture is available, with 1% of organisms resistant to all commonly available oral classes. Multidrug resistance in patients with an outpatient urine culture is associated with a significantly increased risk of treatment failure and subsequent hospitalization. Doxycycline (DOX) and fosfomycin (FOS) are orally available alternatives demonstrating their efficacy is limited.

Table 1: Outcomes of patients with CRE UTI treated with Fosfomycin and Doxycycline

| Outcomes | Fosfomycin n=14 | Doxycycline n=8 | p-value |
|----------|-----------------|-----------------|---------|
| Clinical Cure | (percentage)     | (percentage)     |         |
| 3(1) (%) | 0 (0%) | 0 (0%) | 0.0122 |
| Microbiological Failure | (30%) | (25%) | 0.6248 |
| Persistent infection | (30%) | (24%) | 0.9999 |
| 30 day relapse | (0%) | (5%) | 0.0564 |
| Readmission due to CRE | (0%) | (3%) | 0.8436 |
| In hospital mortality/discharge to hospiz | (1(1) | (1(2) | >0.9999 |
| Adverse reaction | (1(1) | (0%) | 0.001 |

1. The patient had a prior dose of hemodialysis, intradialytic dialyzer filtered CRE cultures. Outcomes from other facilities were excluded.

1529. Suprapubic Catheter Placement Improves Antimicrobial Stewardship in a Veterans Affairs Long-term Care Facility

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Session: 150. Urinary Tract Infection
Friday, October 5, 2018: 12:30 PM

Background. It is unknown if suprapubic catheters (SCs) offer benefit over indwelling urethral catheters (IUCs) in incidence of asymptomatic bacteriuria and catheter-associated infection (CAUTI), or subsequent antibiotic exposure.

Methods. We conducted a retrospective cohort study of unique patients with SCs placed at VA Pittsburgh Healthcare System from February 2015 to March 2018, who had a prior IUC (>20 days for each). Demographic, laboratory, microbiologic, and antibiotic use were compared over the same number of days between IUC and SC periods. IDSA Guidelines were used to define CAUTI and asymptomatic bacteriuria.

Results. Eighteen patients with SC were included. SCs were in place for a median of 213 days (range: 49–1,085). The indications for catheterization were urinary retention (n = 12), neurogenic bladder (n = 5), and decubitus healing (n = 1). The most common underlying conditions were benign prostatic hyperplasia (n = 9), multiple sclerosis (n = 2), and Parkinson’s disease (n = 2). The median number of urine cultures collected per 100 IUC days and 100 SC days were 2.28 (range: 0–4.08) and 0.35 (range: 0–5.85), respectively (P = 0.02). Forty-four percent (8/18) and 39% (7/18) received at least one antibiotic course for asymptomatic bacteriuria during IUC and SC periods. A total of 170 days of antibiotic therapy were given for asymptomatic bacteriuria per 4,881 IUC days vs. 107 days for asymptomatic bacteriuria per 4,881 SC days (P = 0.0001). The median rate of CAUTI was 0.25 per 100 IUC days vs. 0.08 per 100 SC days (P = 0.15). The most common pathogens causing CAUTI were Pseudomonas aeruginosa (n = 5), Candida albicans (n = 2), Klebsiella pneumoniae (n = 1) and Enterococcus faecalis (n = 1). A total of 163 days of antibiotic therapy were given for CAUTI per 4,881 IUC days vs. 38 days of antibiotic therapy for CAUTI per 4,881 SC days (P = 0.0001).

Conclusion. SCs were associated with significantly less overall antibiotic exposure than IUCs, both as treatment of CAUTIs and as inappropriate agents against asymptomatic bacteriuria. CAUTI rates were similar among patients with SCs and IUCs, although cultures were performed more often in those with IUCs. Reducing the treatment of asymptomatic bacteriuria remains a leading stewardship challenge.

Disclosures. All authors: No reported disclosures.