Current oral (PO) regimen options are suboptimal for hospitalized patients with urinary tract infections (UTI) due to contemporary resistant Enterobacteriaceae (ENT): A multicenter analysis

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ABSTRACT

Background: We evaluated empiric intravenous (IV) and IV to PO regimen prescriptions in UTI admissions by ESBL and fluoroquinolone susceptibility (FQ NS, FQ S). Material/methods: We analyzed the first positive ENT urine culture ≤ 3 days from admission in those with a discharge primary or secondary UTI ICD10 code from 68 US hospitals from October 2015 - 2017 (BD Insights, Franklin Lakes, NJ). We identified IV antibiotics of duration ≥ 24 hrs as empiric if started < 5 days prior to final result & PO regimen as conversion to PO after 24 hours of IV therapy. Empiric & PO regimens were evaluated by ESBL, FQ S, and FQ NS status. The Fisher's exact test was used to test for significance. Results: A total of 16,102 adult inpatients (mean age 69.5 years; 77.7% female) with culture positive ENT UTI were identified: 11.0% (n=1763) were ESBL +, 31.3% (n=5017) were FQ NS and 8.9% (n=1433) were both ESBL+ & FQ NS. IV to PO was more common in susceptible vs. non-susceptible UTIs as follows: 25.1% vs. 12.1% for ESBL+ vs. ESBL-, 15.6% vs. 12.9% for FQ S vs. FQ NS, and 15.5% vs. 10.9% for ESBL/FQ-S vs. ESBL+FQ NS, p < .001 for all. Compared to admissions with ESBL + FQ NS or FQ S, ESBL-FQ S UTI, carbapenem were more commonly empiric therapy and nitrofurantoin, TMP/SMX and fosfomycin were more common IV to PO regimens. Conclusions: Among patients with resistant UTIs, a large percentage receive an inappropriate IV and/or PO antibiotic unlikely to be active against the cultured pathogen. The current options for PO antibiotic therapy may not be optimal for treatment of resistant UTIs.

INTRODUCTION

Fluoroquinolone non-susceptible and/or ESBL+ Enterobacteriaceae are an increasingly common cause of urinary tract infections among hospitalized patients in the US.¹

These strains are generally susceptible to intravenous (IV) carbapenems, but there are very limited options available for oral antibiotic therapy. This complicates the transition of care from the inpatient to the outpatient setting, leading to increased hospital length of stay (LOS) and higher costs.

We evaluated empiric intravenous (IV) and IV to PO regimens prescribed for patients admitted with known or suspected UTIs caused by ESBL-positive and -negative pathogens based on fluoroquinolone susceptibility (FQ NS, FQ S).

METHODS

- We analyzed all adult hospitalized patients with a primary or secondary discharge diagnosis of UTI (ICD10 codes) who also had a positive urinalysis for the following Enterobacteriaceae (ENT) within 3 days of admission: Escherichia coli, Klebsiella pneumoniae, Klebsiella oxytoca. Proteus mirabilis, Enterobacter cloacae, and Enterobacter aerogenes.²
- Patients from 68 US acute care hospitals in the period between 2015-2017 were included (BD Insights Research Database, Franklin Lakes, NJ USA). (Former CareFusion Research Database).
- Resistant phenotypes were identified as, where applicable: ESBL: confirmed as ESBL-positive per commercial panels or intermediate/resistant to extended spectrum cephalosporins (either ceftriaxone, cefotaxime, cefazidine or cefepime).
- Quinolone NS: intermediate or resistant to ciprofloxacin, levofloxacin or moxifloxacin.
- Patient characteristics and outcomes were categorized by ESBL and FQ susceptibility status in patients that received IV and/or PO antibiotic therapy.
- We identified UTI episodes with any antibiotic started within 5 days prior to day of final culture result with a duration ≥ 24 hours, including within 24 hours prior to admission (e.g. E.R.).
- IV to PO during hospitalization was identified as conversion to a PO antibiotic with a duration of at least 24 hours after IV antibiotic therapy of at least 24 hours in duration.
- Empiric IV and PO regimens were compared according to the ESBL status and fluoroquinolone susceptibility of the isolated pathogen.
- The Fisher’s exact test was used to test for significance.

RESULTS

- A total of 16,022 adult inpatients (mean age 69.5 years; 77.7% female) with culture positive ENT UTI were identified: 11.0% (n=1763) were ESBL +, 31.3% (n=5017) were FQ NS and 8.9% (n=1433) were both ESBL+ & FQ NS.
- IV to PO was more common in susceptible vs. non-susceptible UTIs as follows: 15.1% vs. 12.1% for ESBL- vs. ESBL+, 15.6% vs. 12.9% for FQ S vs. FQ NS, and 15.5% vs. 10.9% for ESBL-/FQ S vs. ESBL+/FQ NS, p < .001 for all.
- Among patients with UTI caused by resistant pathogens (ESBL + FQ NS or NS FQ) as follows: 15.1% vs. 12.1% for ESBL- vs. ESBL+, 15.6% vs. 12.9% for FQ S vs. FQ NS, and 15.5% vs. 10.9% for ESBL-/FQ S vs. ESBL+/FQ NS.

CONCLUSIONS

- Antimicrobial resistance is common in patients hospitalized with UTI.
- Antimicrobial resistance complicates empirical antibiotic therapy. Among patients with resistant UTIs, a large percentage receive an IV and/or PO antibiotic unlikely to be active against the cultured pathogen.
- Urinary tract infection with antibiotic-resistant Enterobacteriaceae is associated with a lower rate of transition from IV to PO antibiotic therapy, suggesting that the current options for PO antibiotic therapy may not be optimal for treatment of resistant UTIs.
- There is an unmet need for new oral options with activity against resistant UTI pathogens to improve the transition of care from inpatient to outpatient setting.

REFERENCES


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