Poster # 140

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 regimens prescribed 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 1, 2015-2017 (BD Insights, Franklin Lakes, NJ). We identified IV antibiotics of duration > 24 hrs as empiric if started < 5 days prior to final culture 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 16,022 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. Compared to admissions with ESBL + /FQ NS or FQ NS vs. ESBL -/FQ S UTI, carbapenems were more commonly prescribed as 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 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.[2] 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 to hospital with urinary tract infections caused by ESBL-positive and -negative pathogens and 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 urine culture for the following Enterobacteriaceae (ENT) within 3 days of admission: *Escherichia coli*, *Klebsiella pneumoniae*, *Klebsiella oxytoca*, *Proteus mirabilis*, *Enterobacter cloacae*, and *Enterobacter aerogenes.*[3]
- Patients from 68 US acute care hospitals in the period between 2015-2017 were included (BD Insights Research Database, Franklin Lakes, NJ USA). [formerly CareFusion Research Database]).
- Resistant phenotypes were identified as, where applicable:
  - ESBLs: confirmed as ESBL-positive per commercial panels or intermediate/resistant to extended spectrum cephalosporins (either ceftriaxone, cefotaxime, ceftazidime or cefepime).
  - Quinolone NS: intermediate or resistant to ciprofloxacin, levofloxacin or moxifloxacin.
- Patient characteristics and outcomes were categorized by ESBL and FQ resistance status in patients that received IV and/or PO antimicrobial therapy.
- We identified UTI episodes with any antibacterial 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 & 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=1,763) were ESBL +, 31.3% (n=5,017) were FQ NS and 8.9% (n=1,433) 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 FQ NS) as compared to susceptible pathogens (ESBL -/FQ S), carbapenems were more commonly prescribed as empiric therapy and nitrofurantoin, TMP/SMX and fosfomycin were more common IV to PO regimens.

TABLE 1. US HOSPITAL CHARACTERISTICS.

BD Sites: n=68	
Region	
Northeast	5 (7.4%)
South	32 (47.1%)
Midwest	26 (38.2%)
West	5 (7.4%)
Urban/Rural	
Urban	62 (91.2%)
Rural	6 (8.8%)
Medical School Affiliation	
Major	4 (5.9%)
Limited	12 (17.6%)
Graduate	2 (2.9%)
No Affiliation	50 (73.5%)
Bed size	
<100	12 (17.6%)
100-300	27 (39.7%)
>300	29 (42.6%)

Short-term acute hospitals: Acute & Critical Access, excludes Children's & Specialty sites

TABLE 2. DISTRIBUTION OF EMPIRIC IV AND ORAL ANTIMICROBIALS UTILIZED IN PATIENTS INITIALLY TREATED WITH IV ANTIMICROBIAL THERAPY.

Treatment	FQ NS	FQ S	ESBL +	ESBL -	ESBL+/FQ NS	ESBL -/ FQ S
IV Empiric Therapy (Total)	4,076	8,677	1,455	11,298	1197	8510
Ceftriaxone	1,609 (39.5%)^¥§	4,271 (49.2%)	458 (31.5%)ϕ	5,422 (48.0%)	348 (29.1%)*	4195 (49.3%)
Piperacillin/Tazobactam	662 (16.2%)	1,294 (14.9%)	223 (15.3%)	1,733 (15.3%)	189 (15.8%)	1,279 (15.0%)
Levofloxacin	432 (10.6%)^	983 (11.3%)	132 (9.1%)ϕ	1,283 (11.4%)	99 (8.3%)*	963 (11.3%)
Cefepime	296 (7.3%)¥§	527 (6.1%)	98 (6.7%)	725 (6.4%)	82 (6.9%)	526 (6.2%)
Meropenem	504 (12.4%)^¥§	389 (4.5%)	333 (22.9%)ϕ	560 (5.0%)	297 (24.8%)*	365 (4.3%)
Ciprofloxacin	207 (5.1%)	506 (5.8%)	61 (4.2%)ϕ	652 (5.8%)	47 (3.9%)*	496 (5.8%)
Ertapenem	108 (2.6%)^¥§	89 (1.0%)	149 (10.2%)ϕ	125 (1.1%)	142 (11.9%)*	85 (1.0%)
IV to PO Regimens (Total)	648	1,719	214	2,153	156	1676
Ciprofloxacin PO	57 (8.8%)¥§	577 (33.6%)	29 (13.6%)ϕ	605 (28.1%)	8 (5.1%)*	558 (33.3%)
Levofloxacin PO	62 (9.6%)¥§	427 (24.8%)	38 (17.1%)	451 (20.9%)	21 (13.5%)	414 (24.7%)
Cephalexin PO	124 (19.1%)^	326 (13.7%)	7 (3.3%)ϕ	353 (16.4%)	6 (3.8%)*	238 (14.2%)
TMP/SMX PO	130 (20.1%)¥§	166 (9.7%)	54 (25.2%)ϕ	242 (11.2%)	45 (28.8%)*	161 (9.6%)
Nitrofurantoin PO	116 (17.9%)^¥§	68 (4.0%)	54 (25.2%)ϕ	13 (6.0%)	51 (32.7%)*	66 (3.9%)
Fosfomycin PO	16 (2.5%)^¥§	4 (0.2%)	15 (7.0%)ϕ	5 (0.2%)	12 (7.7%)*	2 (0.1%)

* p < .0071 ESBL+/FQ NS vs. ESBL-/FQ S; ^ p < .0205 FQ NS vs. ESBL +/FQ NS; ¥ p < .0229 FQ NS vs. ESBL-/FQ S; § p<.012 FQ NS vs FQ S;ϕ p<.0128 ESBL+ vs ESBL-

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 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.

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