A Prospective, Stewardship-Driven IV to PO Antibiotic Conversion For Uncomplicated Bacteremia

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Background

Recent data has shown a transition to oral (PO) antibiotics (ABX) for definitive treatment of uncomplicated bacteremia has similar efficacy compared to continuation of intravenous (IV) ABX, and reduces hospital length of stay (LOS)[1-3].The purpose of this study was to evaluate the safety and efficacy of an antimicrobial stewardship pharmacist-driven, IV to PO ABX transition in clinically stable patients with uncomplicated bacteremia, and to determine the impact on hospital LOS.

Study Design

- A prospective, interventional study with concurrent controls
- Study period: November 23rd 2019 – April 15th 2020
- Statistical analyses: chi-squared for categorical data; t-test for continuous, parametric data; Mann-Whitney U test for continuous, non-parametric or ordinal data

Primary Outcomes of Interest

- 30-day composite **clinical outcome:** all-cause mortality, readmission due to infectious- or antibiotic-related complications, recurrent infection/bacteremia with the same organism recovered
- **Overall hospital length of stay**
- **Hospital length of stay after definitive ABX regimen established:** defined as the final change in ABX occurring prior to patients' discharge

Methods

1. Positive blood cultures were reviewed Monday through Friday using TheraDoc®
2. Patients were evaluated to determine if inclusion and exclusion criteria were satisfied
3. If all study criteria were satisfied, the pharmacist contacted the patient's provider and made a recommendation to transition from IV to PO ABX
4. If the recommendation was accepted, patients were enrolled in the PO ABX group; if the recommendation was not accepted, patients were enrolled in the IV ABX group

Table 1. Inclusion/Exclusion Criteria

Inclusion Criteria	Exclusion Criteria
• Monomicrobial bloodstream infection • Adequate source control achieved by day 5 • Pitt Bacteremia Score of ≤ 1 by day 5 • Tolerating enteral medications/food by day 5 • At least 1 *in vitro* active oral antibiotic available • At least 1 *in vitro* active antibiotic prescribed within 24 hours of index blood culture	• Receipt of 2nd concomitant *in vitro* active antibiotic beyond day 5 • Indication requiring > 14 days of antibiotic therapy • Blood culture (+) for *Staphylococcus aureus*, Coagulase-negative Staphylococci, Fungi, or other organisms documented as contaminants • > 50% of index blood cultures (+) for Enterococci • ANC < 1,000 cells/mm^3

Table 2. Baseline Characteristics

N (%) for all data unless otherwise noted	IV group (N=23)	PO group (N=46)	P-value
Female	11 (48)	25 (57)	> 0.05
Age *Median (IQR*)*	74 (68-78)	67 (53-82)	> 0.05
Urinary Tract as Source	9 (39)	36 (78)	**0.01**
Admission to ICU	5 (22)	3 (7)	> 0.05
Hypotensive at Admission	4 (17)	15 (32)	**< 0.00001**
Pitt Bacteremia Score Day 1 *Median (IQR*)*	1 (0-1)	1 (0-2)	> 0.05
Medical Comorbidities^	11 (48)	18 (39)	> 0.05

*IQR – Interquartile Range
^Medical Comorbidities – End-stage liver/kidney disease, structural lung disease, diabetes, HIV, congestive heart failure, solid organ transplant, or hematopoietic stem cell transplant within previous 12 months

Patient Characteristics

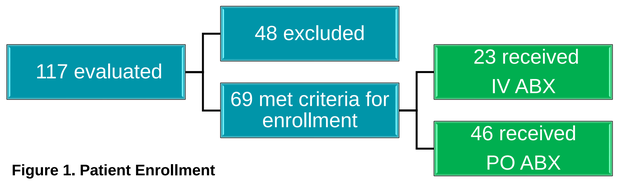

Figure 1. Patient Enrollment

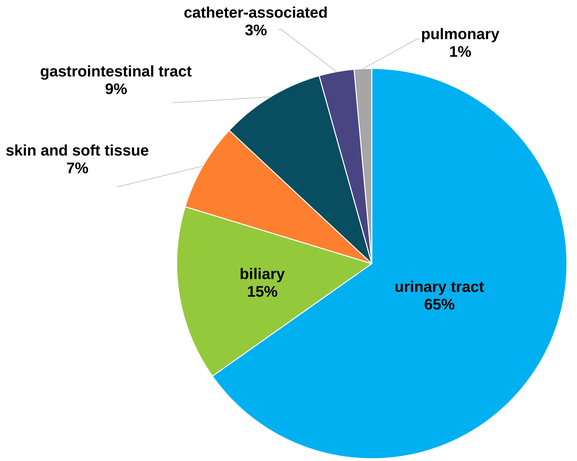

Figure 2. Source of Infection

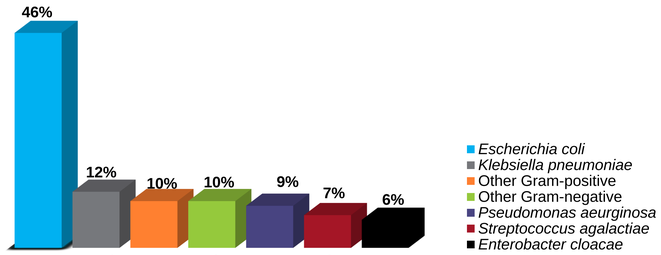

Figure 3. Organisms Recovered

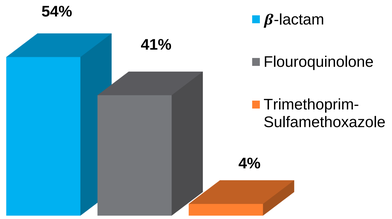

Figure 4. Oral Antibiotics Prescribed

Results

Table 3. Primary Outcomes

N (%) for all data unless otherwise noted	IV (N=23)	PO (N=46)	P-value
30-day Composite Outcome^	1 (4)	1 (2)	**0.61**
Hospital LOS *Median (IQR*)*	8 (5.5-11.5)	5 (4-6)	**0.0004**
Hospital LOS After Definitive ABX Regimen Established *Median (IQR*)*	4 (3-6.5)	0 (0-1)	**< 0.00001**

^30-day composite outcome: all-cause mortality; readmission due to infectious- or antibiotic-related complications; recurrent infection/bacteremia with the same organism recovered
*IQR- interquartile range

Table 4. Secondary Outcomes

N (%) for all data unless otherwise noted	IV (N=23)	PO (N=46)	P-value
Adverse Events Related to ABX / IV Access	0	1 (2)	> 0.05
30-day All-cause Mortality	0	0	-----
30-day Readmission due to Infectious- or ABX-related Complication	1 (4)†	1 (2)^	> 0.05
30-day Recurrent Infection	1 (4)	0	> 0.05
30-day, All-cause Readmission	2 (8)	3 (7)	> 0.05
Central Line Days Avoided per Patient with Switch to oral Antibiotics *Median (IQR*)*	N/A	9 (8-11)	-----
Total Cost of Antimicrobials	$5,008.60	$2,273.31	-----
Estimated Hospital Costs Avoided due to Difference in Length of Stay	N/A	$486,400	-----

†infection with the same organism
^infection with different organism
*IQR- interquartile range

Conclusions

This study demonstrates that effective pharmacist-driven intervention to transition from IV to PO ABX in patients with uncomplicated bacteremia has a significant impact on hospital LOS and healthcare expenditures, with similar clinical outcomes to continued IV therapy.

References

1. Kutob, L.F., et al., *Effectiveness of oral antibiotics for definitive therapy of Gram-negative bloodstream infections.* International journal of antimicrobial agents, 2016. 48(5): p. 498-503.
2. Rieger, K.L., et al., *Intravenous-only or Intravenous Transitioned to Oral Antimicrobials for Enterobacteriaceae-Associated Bacteremic Urinary Tract Infection.* Pharmacotherapy, 2017. 37(11): p. 1479-1483.
3. Tamma, P.D., et al., *Association of 30-Day Mortality With Oral Step-Down vs Continued Intravenous Therapy in Patients Hospitalized With Enterobacteriaceae Bacteremia.* JAMA internal medicine, 2019. 179(3): p. 316-323.