Development and Implementation of a Short Duration of Antibiotic Therapy Algorithm for Uncomplicated Gram-Negative Bacteremia

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Background

- Recent literature suggests no difference in clinical outcomes between short course (7 days) and prolonged course (14 days) antibiotic therapy for the treatment of Gram-negative bacteremia (GNB).[1,2]
- Shorter antibiotic duration may reduce antibiotic-associated adverse events, length of hospital stay, and development of multidrug-resistant organism.[3]
- Based on available literature and expert opinion, an algorithm was developed to assist with identification of patients with uncomplicated GNB eligible for 7 day courses of antibiotic therapy.
- Additional recommendation for IV-to-PO switch was included in the algorithm.

Objectives

- **Primary objective**: Evaluate the impact of the algorithm on duration of therapy
- **Secondary objective**: Evaluate the impact of the algorithm on patient outcomes (listed below)

Methods

Eligibility Criteria for 7-Day Therapy (assessed between day 2 and 5 of therapy)

- **Inclusion criteria**: Adults with blood cultures positive for one or more of the following organisms: *E. coli, Klebsiella* spp., *Enterobacter* spp., *Serratia* spp., *Proteus* spp., *Citrobacter* spp., *Morganella* spp., *Providencia* spp., *Hafnia alvei*, *Pantoea agglomerans.*
- **Exclusion criteria**:
  - Lack or inadequate source control by day 5
  - History of solid organ transplant (SOT)
  - History of stem cell transplant in previous 12 months
  - Current or expected neutropenia (ANC < 500 cells/mm^3) for next 2 weeks
  - Bone/joint, CNS, or endocarditis/endovascular involvement
  - Persistent fever or vasopressor/fluid resuscitation
  - Polymicrobial bacteremia with Gram-positives or anaerobes

Algorithm Implementation and Stewardship Intervention

- Starting 11/11/2019, the algorithm became available in the institution-specific antibiotic guidelines app and medical and pharmacy staff were notified via email.
- The antibiotic stewardship program reviewed cases of GNB on weekdays and contacted the relevant provider (e.g., clinical specialist pharmacist, ID consult service or primary team) to determine the plan for duration of therapy and recommend 7 days of therapy and IV-to-PO conversion based on the algorithm.

Study Outcomes

- **Primary outcome**: Duration of therapy for GNB
- **Secondary outcomes**: Duration of IV antibiotic therapy, length of hospital stay, 30-day recurrence of bacteremia, 90-day *C. difficile* infections and multidrug-resistant organism infections, 30-day antibiotic-related adverse events

Methods, *cont.*

Study Design

Before-after study comparing data from the baseline (11/11/2018 to 3/31/2019) and intervention (11/11/2019 to 3/31/2020) periods.

Statistical Analysis

Categorical values were analyzed using χ^2 test and continuous values were analyzed using Mann-Whitney U test or Student's t-test

Results

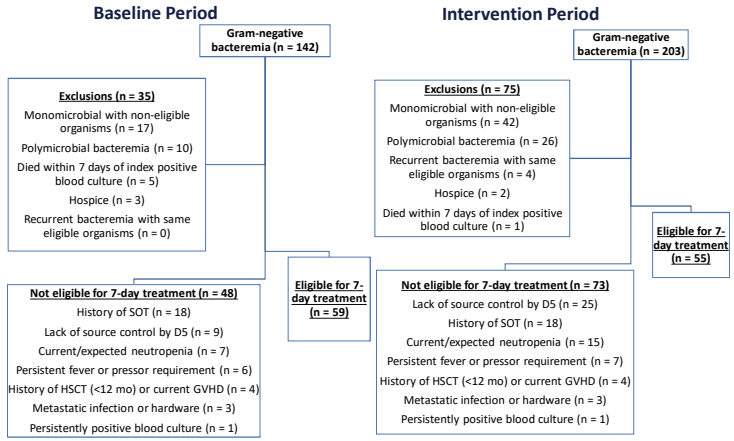

Table 1: Baseline Characteristics of Patients

Characteristics	Baseline (n = 59)	Intervention (n = 55)	P Value
Age, median (IQR), years	60 (46-71)	62 (51-70)	0.16
Charlson Comorbidity Score, median (IQR)	6 (4-10)	6 (2-8)	**0.03**
Pitt Bacteremia Score, median (IQR)	1 (0-2)	1 (0-2)	0.19
Immunocompromise[a], No. (%)	13 (22.0)	12 (21.8)	0.64
Source of bacteremia, No. (%)			
Urinary	27 (45.8)	22 (40.0)	0.64
Biliary	6 (10.2)	14 (25.5)	0.05
Intraabdominal	12 (20.3)	14 (25.5)	0.57
Catheter-associated	11 (18.6)	2 (3.6)	**0.02**
Others	3 (5.1)	3 (5.4)	--

[a]Chemotherapy within previous 6 months and/or immunomodulatory therapy within previous 30 days

Results, *cont.*

Table 2: Organisms

Bacteremia organism, No. (%)	Baseline (n = 59)	Intervention (n = 55)	P Value
Escherichia coli	29/64 (45.3)	30/59 (50.8)	0.66
Klebsiella pneumonia	20/64 (31.3)	12/59 (20.3)	0.24
Klebsiella oxytoca	0	4/59 (6.8)	--
Klebsiella (Enterobacter) aerogenes	3/64 (4.7)	1/59 (1.7)	0.36
***Enterobacter* spp.**	6/64 (9.4)	4/59 (6.8)	0.60
***Serratia* spp.**	3/64 (4.7)	4/59 (6.8)	0.63
Others	3/64 (4.7)	4/59 (6.8)	0.64
ESBL-producer	7/64 (10.9)	8/59 (13.6)	0.66

Table 3: Outcomes

Outcomes	Baseline (n = 59)	Intervention (n = 55)	P Value
Duration of therapy, median (IQR), days	10.0 (7-14)	8.0 (7-10.5)	0.04
Duration of IV therapy, median (IQR), days	7.0 (4-8.5)	4.0 (3-7)	0.004
Length of stay, median (IQR), days	7.0 (5-9)	4.0 (3-9.5)	0.029
Recurrent bacteremia, 30-day, No. (%)	2 (3.4)	1 (1.8)	0.60
All-cause mortality, 30-day, No. (%)	2 (3.4)	3 (5.5)	0.59

Table 4: Infectious Disease Pharmacists Interventions

7-day therapy	**Interventions made, No. (%)**	34 (61.8)
	Interventions accepted, n/N (%)	25/34 (73.5)
	Interventions unnecessary, No. (%)	16 (29.0)
IV-to-PO switch	**Interventions made, No. (%)**	21 (38.2)
	Interventions accepted, n/N (%)	18/21 (85.7)
	Interventions unnecessary, No. (%)	29 (52.7)

Conclusion

Implementation of a treatment algorithm related to duration of therapy for GNB successfully shortened duration of therapy and hospitalization, and increased conversion from IV-to-PO antibiotic therapy.

References

1. Chotiprasitsakul D et al. Comparing the outcomes of adults with Enterobacteriaceae bacteremia receiving short-course versus prolonged-course antibiotic therapy in a multicenter, propensity score-matched cohort. *Clin Infect Dis.* 2018;66(2):172-7. doi:10.1093/cid/cix767.
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3. Corey GR, Stryjewski ME, Everts RJ. Short-course therapy for bloodstream infections in immunocompetent adults. *Int J Antimicrob Agents.* 2009;34 Suppl 4:S47-51.