Intravenous-to-Oral Antibiotic Stepdown for Uncomplicated Streptococcal Bacteremia

Madison Salam, PharmD; Cynthia Nguyen, PharmD, BCIDP; Natasha Pettit, PharmD, BCPS, BCIDP; Jennifer Pisano, MD; Alison Lew, PharmD, BCIDP
The University of Chicago Medicine

AT THE FOREFRONT UChicago Medicine

Background

- Bloodstream infections (BSIs) are estimated to be the 7th leading cause of death in the United States.[1]
- Intravenous (IV) antibiotic use is associated with catheter-associated infections, thromboses, longer hospital stay, and increased treatment cost as compared to oral (PO). [2]
- Studies in Gram-negative BSI have shown similar mortality and infection rates for IV-to-PO stepdown when high bioavailability agents are used[3-6]
- Data for IV-to-PO stepdown in Gram-positive infections are limited

Objective

To compare the efficacy and safety of IV versus IV-to-PO stepdown therapy for uncomplicated Streptococcal bloodstream infections

Outcomes

- Primary: clinical success, defined as composite of absence of recurrence, infection-related readmission, and infection-related mortality at 90 days.
- Secondary: 90-day infection recurrence, 90-dayinfection-related readmission, 90-day infection-related mortality, 90-day all-cause mortality, 30-day microbiological success, length of stay, IV-line associated complications, antibiotic associated adverse events

Methods

- Design: retrospective non-inferiority, single center
- Inclusion: ≥18 years, positive blood culture for *Streptococcus* species with reported susceptibilities, ≤48 hours of positive blood cultures, received treatment.
- Exclusion: Complicated infection (unattainable source control, endovascular infection, bone/joint involvement, or CNS infection), polymicrobial bacteremia, or mortality prior to the completion of treatment

Results

Table 1: Baseline Characteristics

Characteristic	IV (n=36)	IV-to-PO (n=45)	P-value
Age (Median [IQR])	59 [44 – 68]	56 [46 – 71]	0.625
Male (n,%)	16 (44)	29 (54)	0.089
BMI (Median [IQR])	27.5 [23.0 – 35.1]	26.6 [21.2 – 33.0]	0.651
Pitt Bacteremia Score (Median [IQR])	0 [0 - 2]	1 [0 – 2]	0.425
Charlson Comorbidity Index (Median [IQR])	4 [2.5 – 5]	5 [3 – 6]	0.365
ICU Admission at Positive Blood Culture (n,%)	10 (28)	5 (11)	0.083

Table 2: Definitive PO Regimens

Regimen		N (%)
Amoxicillin	500 mg q8 1000 mg q8	1 (2) 3 (7)
Amoxicillin/Clavulanate	875 mg q12	20 (44)
Cephalexin	1000 mg q12	5 (11)
Cefdinir	300 mg q12	11 (24)
Levofloxacin	750 mg q24	4 (9)
Clindamycin	300 mg q8	1 (2)

Figure 1: Source of Infection

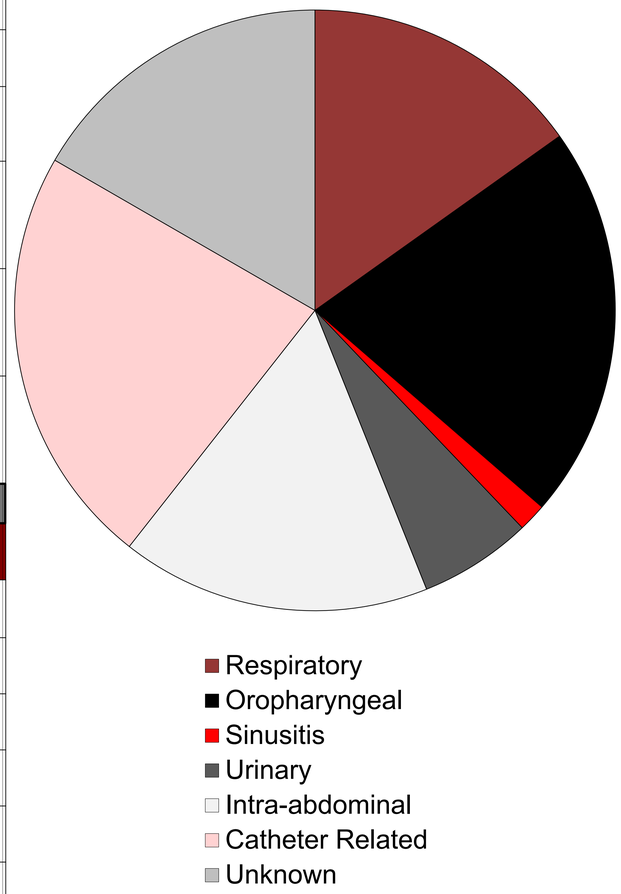

Table 3: Endpoints

Endpoint	IV (n=36)	IV-to-PO (n=45)	OR (90% CI)	P-value
Primary Composite (n, %)	34 (94)	41 (91)	1.66 (0.38 – 7.25)	0.573
Infection-Related Mortality (n, %)	0 (0)	0 (0)	n/a	n/a
Infection Recurrence (n, %)	0 (0)	0 (0)	n/a	n/a
Infection-related Readmission (n, %)	2 (6)	4 (9)	3.00 (0.62 – 14.49)	0.251
Line Complications (n, %)	5 (14)	0 (0)	n/a	**0.015**
Antibiotic Duration, Days Median [IQR]	14.1 [12.59, 14.43]	13.7 [12.5 – 15.8]	1.59 (-19.9 0 – 23. 06)	0.902
Length of Stay, Days Median [IQR]	11.0 [6.5 – 20.5]	6.0 [4.0 – 8.0]	-9.1 (-12.56 – -5.65)	**<0.001**

Discussion

- Baseline characteristics did not differ significantly between groups, although ICU admission was numerically more frequent in the IV group
- Similar to new data in Gram-negative bloodstream infections, this study showed similar clinical outcomes of IV-to-PO stepdown compared to IV therapy
- Length of stay and IV-line associated complications may be decreased with the shortened duration of IV therapy
- Differences in clinical outcomes between oral agents evaluated in this study, and require further evaluation
- Strict exclusion criteria make this study more applicable to less complicated patients and infections, and should be interpreted as such in clinical practice
- No outcome met our prespecified noninferiority margin of 10%, attributed to the small sample size

Limitations

- This single center analysis may not accurately reflect patient and infection characteristics at all centers
- Variation in antimicrobial selection may have influenced results
- Additionally, the small sample size does not meet power for the predetermined noninferiority threshold.

Next Steps

- Plan to expand to a multicenter study to asses a larger patient population
- Data collection is ongoing but is projected to meet power for non-inferiority with a total of at least 224 patients

References

1. Goto M, Al-Hasan MN. *Clin Microbiol Infect*. 2013 Jun;19(6):501-9.
2. Li HK, et al. *PLoS Med* (2015)12(5): e1001825.
3. Punjabi C, et al. *Open Forum Infect Dis* 6:364, 2019.
4. Tamma PD, et al. *JAMA Intern Med* 179(3):316-323, 2019.
5. Kutob LF, et al. *Int J Antimicrob Agents* 48:498 –503, 2016.
6. Mercuro NJ, et al. *Int J Antimicrob Agents* 51:687– 692.

Disclosures

The authors of this presentation have no financial interests with commercial entities that may have a direct or indirect interest in the subject matter of this presentation