

Evaluation of Early Oral Antibiotic Step Down Therapy in Uncomplicated Streptococcus Bacteremia

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Background

- In uncomplicated gram-negative bacteremia, oral step down therapy has similar mortality and recurrence of bacteremia but with shorter hospital length of stay as continued intravenous therapy.¹
- There is limited literature on oral antibiotic step down therapy in streptococcus bacteremia.²
- Early oral step down antibiotic therapy may lead to decreased healthcare costs, lower amounts of hospital- and line-associated complications, and better allocation of healthcare resources.²

Objective

- Evaluate the clinical outcomes of intravenous to oral step down antibiotic therapy in uncomplicated streptococcal bloodstream infections

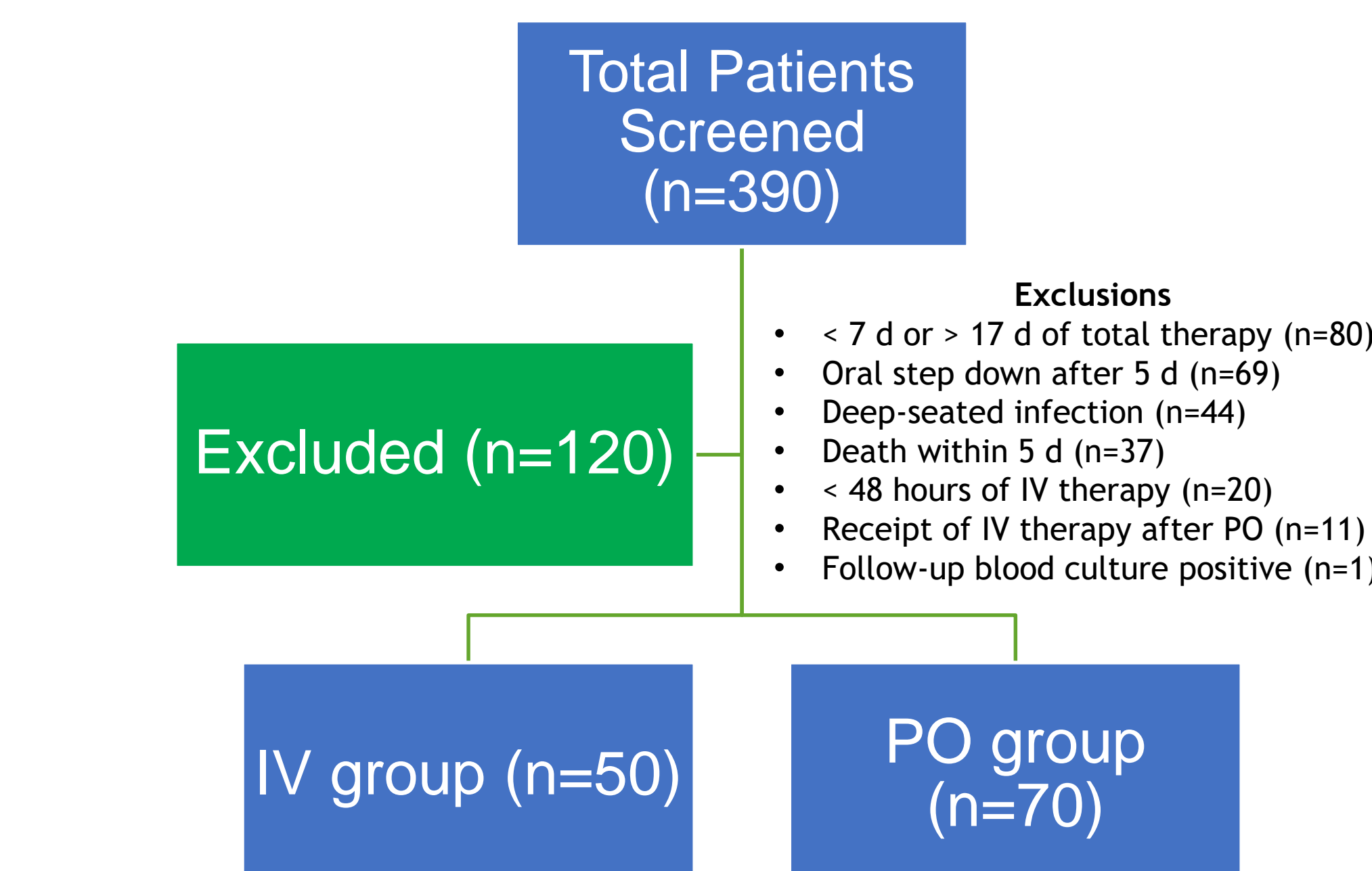
Outcomes

- Primary outcomes
 - 30-day all-cause mortality
- Secondary outcomes
 - 30-day recurrence in bacteremia
 - 30-day rehospitalization
 - Total length of stay in hospital

Methodology

- Retrospective cohort study
- January 1, 2019 to July 31, 2022
- Blood culture data acquired from Baptist Health microbiology labs
- Statistical tests performed on JASP 0.17.1
- Mann-Whitney U and independent t-test performed for continuous and ordinal variables
- Chi square test and Fisher's exact test performed for nominal variables
- Alpha level set at 0.05 for significance

Methodology & Results



Inclusion criteria

- Streptococcus pneumoniae*, Group A Strep, or Group B Strep in 1 or more blood cultures
- Eligible for IV to oral step down in 5 days (PBS < 1, source control, active oral antibiotic available, patient tolerating oral medications)

Exclusion Criteria

- Pitt Bacteremia Score > 1 at day 5
- Receiving < 7 days or > 16 days of total antibiotic therapy
- Oral antibiotics started after more than 5 days of IV antibiotics
- < 48 hours of initial IV antibiotic therapy
- Follow-up cultures being positive by day 4
- Death within the first 5 days
- Deep-seated infections including endocarditis, necrotizing soft tissue infection, meningitis, or osteomyelitis

Baseline Characteristics

| Characteristic | PO (n=70) | IV (n=50) | P-value |
|---------------------------------|-------------------|------------------|---------|
| Age (yrs), mean (SD) | 59.6 (16.7) | 63.4 (14.9) | 0.202 |
| Male, n (%) | 38 (54.3) | 24 (48) | 0.497 |
| Weight (kg), median (IQR) | 83.8 (67.4-106.5) | 92.1 (75.6-92.1) | 0.228 |
| Race/Ethnicity | | | |
| White, n (%) | 56 (80) | 40 (80) | 1.000 |
| Black, n (%) | 14 (20) | 8 (16) | 0.577 |
| Asian, n (%) | 0 (0) | 1 (2.0) | 0.417 |
| American Indian, n (%) | 0 (0) | 1 (2.0) | 0.417 |
| Comorbidities | | | |
| Immunocompromised*, n (%) | 2 (2.9) | 3 (6.0) | 0.648 |
| Charlson Comorbidity Index** | 3 (1-5) | 4 (2-5) | 0.188 |
| COVID-19, n (%) | 5 (7.1) | 3 (6) | 1.000 |
| End Stage Renal Disease, n (%) | 2 (2.9) | 4 (8) | 0.203 |
| Liver Dysfunction, n (%) | 0 (0) | 3 (6.0) | 0.070 |
| Diabetes, n (%) | 20 (28.6) | 22 (44.0) | 0.081 |
| Congestive Heart Failure, n (%) | 12 (17.1) | 11 (22.0) | 0.505 |

*Defined as HIV, Chemotherapy within 6 months, ANC<500/mL, immunomodulatory therapy or steroids within 30 days, solid organ transplant, hematopoietic stem cell transplant within 12 months

**Reported as median (25th percentile - 75th percentile)

IV = intravenous, PO = by mouth

Treatment Characteristics

| Characteristic | PO (n=70) | IV (n=50) | P-value |
|---|------------|------------|---------|
| Day 1 Pitt Bacteremia Score, median (IQR) | 0 (0-0) | 1 (0-2) | 0.021 |
| Day 5 Pitt Bacteremia Score, median (Range) | 0 (0-0) | 0 (0-1) | 0.014 |
| ICU on Admission, n, (%) | 16 (22.9) | 19 (38.0) | 0.072 |
| Infectious Diseases Consult, n (%) | 30 (42.9) | 36 (72.0) | 0.002 |
| Total intravenous days of therapy, median (IQR) | 4 (3-4.8) | 14 (14-16) | <0.001 |
| Total antibiotic days of therapy, median (IQR) | 14 (11-15) | 14 (14-16) | 0.021 |
| Source of Infection | | | |
| Pulmonary, n (%) | 50 (71.4) | 19 (38) | < 0.001 |
| Skin and soft tissue, n (%) | 12 (17.1) | 16 (32) | 0.058 |
| Urinary tract, n (%) | 6 (8.6) | 6 (12) | 0.553 |
| Gastrointestinal tract, n (%) | 0 (0) | 7 (14) | 0.002 |
| Endometrium, n (%) | 1 (1.4) | 0 (0) | 1.000 |
| Unknown, n (%) | 2 (2.9) | 2 (4) | 1.000 |
| Organisms Isolated | | | |
| Group A Strep, n (%) | 3 (4.3) | 5 (3.3) | 0.275 |
| Group B Strep, n (%) | 22 (31.4) | 31 (62) | <0.001 |
| <i>S. pneumoniae</i> | 45 (64.3) | 14 (28) | <0.001 |

ICU=intensive care unit

Outcomes

| Outcome | PO (n=70) | IV (n=50) | P-value |
|--|-----------|--------------|---------|
| Primary outcomes | | | |
| 30-day all-cause mortality, n (%) | 2 (2.9) | 4 (8) | 0.233† |
| Secondary outcomes | | | |
| 30-day re-hospitalization, n (%) | 6 (8.6) | 6 (12) | 0.553 |
| 30-day recurrence of bacteremia, n (%) | 6 (8.6) | 2 (4) | 0.466 |
| Total length of stay in hospital in days, median (IQR) | 4 (3-5) | 7 (4.3-12.8) | <0.001 |

†Logistic regression analysis adjusted for ICU on Admission, aOR 0.08-2.92; p=0.43

| Active Oral Antibiotic (n=70) | N, (%) |
|-------------------------------|-----------|
| Levofloxacin | 51 (72.9) |
| Cefdinir | 11 (15.5) |
| Other*** | 8 (11.6) |

***Other antibiotics include moxifloxacin, amoxicillin/clavulanate, cephalexin, cefuroxime, linezolid (n=2, n=2, n=2, n=1, n=1)

Discussion

- Results corroborate with other studies
 - No increase in mortality in the PO group
 - No difference in recurrence of bacteremia or rehospitalization
 - Shorter length of stay in hospital
- Only pathogenic species of streptococcus were included minimizing bias of assessing contaminated blood cultures
- Most commonly used oral antibiotic was levofloxacin which is 100% bioavailable
- Initial 48 hour intravenous antibiotic lead in was used in every patients
- Limitations
 - Retrospective analysis
 - Small sample size, inadequate power
 - Adverse effect data was not collected between the two groups
- Future directions may include determining optimal length of therapy

Conclusion

- Uncomplicated Streptococcus bacteremia can be treated with early IV to PO antibiotic step down therapy
- Oral step down therapy did not lead to inferior clinical results but led to a shorter length of stay in hospital
- Favorable economic and health outcomes may be associated with shorter length of stay

References

- Tamma PD, Conley AT, Cosgrove SE, et al. Association of 30-Day Mortality With Oral Step-Down vs Continued Intravenous Therapy in Patients Hospitalized With Enterobacteriaceae Bacteremia [published correction appears in JAMA Intern Med. 2019 Nov 1;179(11):1607]. *JAMA Intern Med.* 2019;179(3):316-323. doi:10.1001/jamainternmed.2018.6226
- Kang A, Beuttler R, Minejima E. Evaluation of step-down oral antibiotic therapy for uncomplicated streptococcal bloodstream infections on clinical outcomes. *Ther Adv Infect Dis.* 2022;9:20499361211073248. Published 2022 Jan 30. doi:10.1177/20499361211073248