Clinical outcomes of Ceftriaxone 1 gram vs. 2 gram daily for the treatment of gram-negative Enterobacteriaceae bloodstream infections

Amal Alhadad, Arya Tehrani, Charisse Surio, Meghan Jeffres PharmD

University of Colorado Anschutz Campus Skaggs School of Pharmacy

Skaggs School of Pharmacy and Pharmaceutical Sciences
UNIVERSITY OF COLORADO
ANSCHUTZ MEDICAL CAMPUS

Background

- Bloodstream infections (BSIs), especially gram-negative infections, have high mortality and morbidity[1]
- *E. Coli, Klebsiella pneumoniae* are the most common organisms in gram-negative bacteremia[2]
- Even though The UCHealth Antibiotic Guide recommend either a dose of 1 or 2 grams every 24 hours, data supporting either dosing regimen is both sparse and inconclusive[3]

Methods

- Retrospective chart review of patients from January 1, 2018 through August 1, 2021 receiving either 1 g every 24 hours or 2 g every 24 hours of intravenous ceftriaxone for gram negative bloodstream infection
- Inclusion: Patients with gram-negative enterobacteriaecae BSI who received empiric ceftriaxone ≥72h (N = 405)
- Exclusion: GN pathogen resistant to ceftriaxone, receipt of both 1 and 2 grams of ceftriaxone for treatment of index GN BSI
- Primary outcome: frequency of treatment failure 72 hours post initiation of therapy
- Secondary outcomes: frequency of CDI, 30-day mortality, and 30-day infection-related readmission

Results

Table 1. Baseline Patient Characteristics

Variable	Ceftriaxone 1g IV q24h, n =168	Ceftriaxone 2g IV q24h, n =237	P value
Age, years ± SD	64.2 ± 19.1	67.2 ± 16.7	.10
Female, n (%)	125 (74.4)	154 (65.0)	.01
Height, cm ± SD	164.3 ± 12.3	167.1 ± 11.3	.02
Weight, kg ± SD	77.1 ± 21.3	83.2 ± 25.0	.01
BMI ± SD	29.1 ± 14.4	29.7 ± 8.9	.61
Race, n (%)			.00
Caucasian or White	97 (57.7)	184 (77.6)	
African American or Black	26 (15.5)	8 (3.4)	
Other/Unknown	45 (26.8)	45 (19.0)	
Quick Pitt Score, mean ± SD	0.79 ± 0.90	0.77 ± 0.92	.88
Source of infection, n (%)			.74
Respiratory	4 (2.4)	2 (0.9)	
Urinary	142 (84.5)	197 (83.8)	
CVC/other intravascular device	1 (0.6)	1 (0.4)	
Other	15 (8.9)	25 (10.6)	
Unknown	6 (3.6)	10 (4.3)	
Empiric duration, days ± SD	3.9 ± 1.3	4.7 ± 2.5	.00
Organism, n (%)	**Ceftriaxone 1g IV q24h, n =168**	**Ceftriaxone 2g IV q24h, n =237**	**P value**
Escherichia coli	148 (88.1)	196 (82.7)	.16
Klebsiella pneumoniae	20 (11.9)	31 (13.1)	.76
Proteus spp.	0 (0.0)	2 (0.8)	.51
Enterobacter cloacae complex	0 (0.0)	1 (0.4)	1.00
Other	1 (0.6)	10 (4.2)	.03

Table 2. Outcomes

Variable	Ceftriaxone 1g IV q24h, n =168	Ceftriaxone 2g IV q24h, n =237	P value
Early clinical failure, n (%)[a]	28 (16.7)	50 (21.1)	.31
Temperature >38°C	19 (11.3)	29 (12.2)	.88
Hemodynamic support	1 (0.6)	5 (2.1)	.41
Respiratory Support	5 (3.0)	14 (5.9)	.23
Transfer to ICU	6 (3.6)	11 (4.6)	.80
Composite secondary outcomes, n (%)	9 (5.4)	21 (8.9)	.25
30-day mortality, n (%)	2 (1.2)	8 (3.4)	.21
Infectious cause of 30-day readmission, n (%)	7 (4.2)	13 (5.5)	.65
CDI infection w/n 60 days of discharge, n (%)	0 (0.0)	1 (0.4)	1.00

Discussion

- No difference in early clinical failure between empiric ceftriaxone 1 g and 2 g in GN BSI
- Ceftriaxone 1 g and 2 g groups were associated with similar 30-day mortality, 30-day infection related readmission, and CDI
- Pyelonephritis was the predominant source of GNI in both groups, higher daily dose is not needed to achieve similar clinical outcomes as 1 g
- Ceftriaxone 2 g daily can be used empirically without higher risk of CDI compared to 1 g daily
- Limitations include retrospective design, single center study

References

1. Alexandraki I, Palacio C. Gram-negative versus Gram-positive bacteremia: what is more alarmin(g)?. *Crit Care*. 2010;14(3):161. doi:10.1186/cc9013
2. Foster MT Jr. Ceftriaxone in treatment of serious infections. Septicemia. *Hosp Pract (Off Ed)*. 1991;26 Suppl 5:43-63. doi:10.1080/21548331.1991.11707743
3. UCHealth—AMC Antimicrobial Stewardship Guide (2021)