



Cefiderocol Use in Burn Patients Admitted to an Intensive Care Unit

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Introduction

- Cefiderocol is a novel cephalosporin that binds to ferric acid and is moved across the outer membrane of Gram-negative bacilli via iron transport
 - This allows cefiderocol to elude typical bacterial resistance mechanisms
- Once through the outer membrane, cefiderocol exerts typical cephalosporin activity
- Cefiderocol has activity against multidrug resistant organisms, including *Acinetobacter* spp. and *Pseudomonas* spp.
- Cefiderocol is relatively safe, but has the potential to predispose to secondary infection with *Clostridioides difficile*
- Recently concerns have been raised with cefiderocol heteroresistance and the potential for clinical failures, particularly in patients infected with carbapenem resistant *Acinetobacter*
- Recovery after burns is frequently threatened by infections with MDR gram-negative organisms that often present therapeutic challenges due to competing considerations (toxicities, drug-drug interactions)
- Cefiderocol presents an attractive option in these clinical scenarios

Objectives

- The objective of this clinical chart review was to describe the use of cefiderocol in critically ill burn patients

Methods

- Clinical chart review
- Review criteria:
 - Admission to burn ICU between September 2019 and April 2022
 - Received cefiderocol during ICU stay
 - Clinical cure was defined as resolution of infecting syndrome or survival to hospital discharge whichever happened first
 - C. difficile* was diagnosed via PCR and compatible clinical syndrome (1 or more loose stools in 24 hours)

Results

- 5 patients receiving 6 courses of cefiderocol were included
- All isolates recovered were carbapenem resistant
- The 2 *E. coli* isolates carried a New Delhi metallo-beta lactamase
- 66.7% (n=4) patients achieved a clinical cure with cefiderocol treatment
- Initial regimens included co-administered polymyxin in 66.7% (n=4) of patients
- 83% (n=5) patients were on CRRT at the time of cefiderocol administration

Table 1. Demographic Characteristics

	N=5
Age, years, median (IQR)	54.5 (43.5, 56.5)
Male gender, n (%)	5 (100%)
Burn size, % TBSA, median (IQR)	47 (31, 60)
Mechanism of injury, n (%)	
Flame burn	3 (60%)
Scald burn	1 (20%)
Blast injury	1 (20%)
Hospital LOS, days, median (IQR)	112 (96.5, 141)
Inhalation injury	2 (40%)
In-hospital mortality	3 (60%)

Table 2. Infection Characteristics

	N=6
Time from injury to cefiderocol, days, median (IQR)	7 (7, 16)
Indication for cefiderocol	
Bacteremia, n (%)	2 (33.3%)
Pneumonia, n (%)	2 (33.3%)
Wound infection, n (%)	1 (16.7%)
Disitis/osteomyelitis, n (%)	1 (16.7%)
CRRT at the time of cefiderocol	4 (66.7%)
Duration of cefiderocol, days, median (IQR)	11.5 (7, 16)

Table 3. Organisms isolated

	N=6
<i>Acinetobacter baumannii</i>	1 (16.7%)
<i>Enterobacter cloacae</i>	1 (16.7%)
<i>Escherichia coli</i>	2 (33.3%)
<i>Pseudomonas aeruginosa</i>	2 (33.3%)

Table 4. Susceptibilities to other agents

	NDM <i>E. coli</i>	NDM <i>E. coli</i>	<i>E. Cloacae</i>	ACB	PsA	PsA
Amikacin	Green	Green	Green	Gray	Green	Green
Aztreonam	Red	Red	Red	Red	Red	Red
Imipenem	Red	Red	Red	Red	Red	Red
Tobramycin	Green	Green	Red	Red	Green	Green
Ceftazidime / avibactam	Red	Red	Red	Gray	Red	Red
Piperacillin / tazobactam	Red	Red	Red	Red	Red	Red
Ceftazidime	Red	Red	Red	Red	Red	Red
Cefepime	Red	Red	Red	Red	Red	Red
Meropenem	Red	Red	Red	Red	Red	Red
Ciprofloxacin	Green	Green	Green	Red	Green	Green

Red – non-susceptible
 Green – susceptible
 Gray – not-tested

PsA: *Pseudomonas aeruginosa*
 ACB: *Acinetobacter baumannii*

Conclusions

- Cefiderocol is a cephalosporin with a novel mechanism of action that can be used to treat MDROs in critically ill burn patients
- No secondary *C. difficile* infections were observed
- Mortality was high in this case series, but likely due to factors including severity of initial burn injury
- Further work, including correlation of cefiderocol MICs to survival or clinical cure, would be helpful