2034

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Outcomes with ceftazidime/avibactam in patients with *Pseudomonas* infections: a multi-center study

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Revised Abstract

Background: Ceftazidime-avibactam (CAZAVI) is a cephalosporin-beta-lactamase inhibitor combination that is active against Enterobacteriaceae and Pseudomonas aeruginosathat is resistant to other agents, including carbapenems and late-generation cephalosporins. This purpose of this study is to describe the outcomes of patients receiving ceftazidime-avibactam for Pseudomonas infections.
Methods: A retrospective chart review was completed from March 2015 through April 2016 at 3 hospitals in the United States for adult patients who received ceftazidime/avibactam for a Pseudomonas infection. Patients were included if they received CAZAVI for at least 24 hours for a carbapenem-resistant Pseudomonas. Dosage was chosen by providers at individual sites. The primary outcome was in-hospital mortality. Microbiologic and clinical outcomes were also evaluated. Microbiological success required a negative culture at the end of therapy. Clinical success was judged by improved symptoms, improved imaging where relevant, and defervesence.
Results: : Overall, 10 patients received ceftazidime-avibactam for a *P. aeruginosa* infection. Twenty-seven percent of cases were bacteremia, 28% urinary tract, and 27% pneumonia. Over half of the patients were in the ICU at the time of receiving ceftazidime-avibactam. In hospital mortality was

Conclusions: In this severely ill population, ceftazidime/avibactam was an appropriate option for patients with multi-drug resistant organisms causing *Pseudomonas* infections.

Background

The incidence of multi-drug resistant (MDR) organisms is increasing, and infections due to drug-resistant pathogens have become endemic in parts of the world, including the United States[1].Ceftazidime-avibactam is a cephalosporin-beta-lactamase inhibitor combination that is approved for complicated urinary tract infections (cUTI) and complicated intra-abdominal infections (cIAI) and has shown efficacy for Enterobacteriaceae and Pseudomonas aeruginosa that may be resistant to other agents, including ceftazidme alone[2, 3]. An observational study was conducted to evaluate the utility of ceftazidime-avibactam for *Pseudomonas* infections from any body site. The results presented are from multiple centers study.

Methods

This is a descriptive case series of patients who received CAZ-AVI for carbapenem-resistant *Pseudomonas* infections. A retrospective chart review was approved by the local institutional review board for each site and was completed from March 2015 through August 2016 at 9 hospital centers for adult patients who received ceftazidime/avibactam for a *Pseudomonas* infection, defined as having an MIC≥2 mcg/mL to imipenem and meropenem. Patients were included if they received ceftazidime/avibactam for at least 24 hours. The primary outcome was in-hospital mortality. Microbiologic and clinical outcomes were also evaluated. Microbiological success required a negative culture at the end of therapy. Clinical success was judged by improved symptoms and defervesence. Each patient was managed individually by the clinicians at the site.
Susceptibility testing to CAZ-AVI was not performed at all sites.

Conclusion

This retrospective case series describes the outcomes of CAZAVI for carbapenem-resistant *Pseudomonas* infections. The number of patients treated was small. Clinical success was observed in 7 of 10 patients, microbiologic cure in 5 of 10 patients, and in hospital mortality occurred in 2 of 10 patients. Further studies evaluating the use of ceftazidime-avibactam in various infections are warranted.

References

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Results

Table 1. Summary of Cases

Case	Age/ Gender	Type of Infection	Medical History	Prior Therapy for *Pseudomonas*	Duration of CAZ-AVI (days)	Susceptibility to CAZAVI	Outcomes
1	72/M	Bone/joint	Anemia, arthritis, depression, GERD b/l THA, Right TKA	Ciprofloxacin	14	Yes	Indeterminate clinical success Microbiologic cure Discharged to SNF
2	70/M	Intra-abdominal	DM, HTN Splenectomy, pancreatectomy	Meropenem, levofloxacin, tobramycin	12	Yes	Clinical success Presumed micro cure Discharged home
3	7/3M	Pneumonia	DM, obesity, gastric ulcer, HTN, stomach cancer, esophageal cancer, eye surgery, tracheostomy	Amikacin, pip/tazo	11	Yes	Clinical success Presumed micro cure Discharged to SNF
4	75/F	Urinary tract	Htn, heart disease, renal disorder, appendectomy	Cefepime	13	Yes	Clinical success Presumed micro cure Deceased
5	75/F	Pneumonia	Htn, BPH, mitral valve regurgitation, low back pain, bowel obstruction	pip/tazo, cefepime, meropenem	1	Not tested	Clinical success Presumed micro cure Discharged home
6	75/M	Pneumonia	TIA, HTN, arthritis, ALS, hyperlipidemia, cholecystectomy, elbow surgery, eye surgery	Tobramycin	4	Not tested	Clinical success Presumed micro cure Discharged home
7	70/F	Pneumonia	Atrial fibrillation, lung transplant (2006), hypothyroid, CDI, chronic renal disease, DM, HTN, COPD, IPF, hiatal hernia, DDD, OSA, GI bleed, neuropathy, valvular heart disease	Amikacin	3	Not tested	Indeterminate clinical success Microbiologic failure Discharged to SNF
8	51/F	Pneumonia, wound, UTI	Multiple sclerosis, VDRF, HTN, CVA, anemia, recurrent UTI and pneumonia, tracheostomy, PEG, left kidney stent	Amikacin, aztreonam	15	Not tested	Clinical failure Microbiologic cure Discharged home
9	73/F	Pneumonia	Stroke, asthma, lung cancer, hypothyroid, atrial fibrillation, DM, pneumonia, depression, GERD, HTN, COPD, G-tube, port-a-cath	Pip/tazo, ceftolozane/tazobactam	7	Yes	Clinical success Presumed micro cure Deceased
10	43/M	Bacteremia	Spinal cord injury and paraplegia from GSW, anemia, cardiomegaly, asthma, ORIF (left femur, humerus) w/ subsequent I&D and antibiotic beads, cholecystectomy, IVC filer, left wrist debridement and hardware (removed)	Amikacin	28	Yes	Clinical success Microbiologic cure Discharged home

Table 2. Patients receiving concomitant antibiotics

Case	Infection Type	Concomitant antibiotics
1	Bone/joint	Ciprofloxacin
2	Intra-abdominal	Amikacin
7	Pneumonia	Amikacin
8	Pneumonia, wound, UTI	Colistin
10	Bacteremia	Amikacin

Table 3. Outcomes

Infection Type	In-hospital Mortality	Clinical Success	Microbiologic Cure
Pneumonia, n/N (%)	1/6 (17)	4/6 (67)	1/6 (17)
UTI, n/N (%)	1/2 (50)	1/2 (50)	1/2 (50)
Bacteremia, n/N (%)	0/1 (0)	1/1 (100)	1/1 (100)
Wound, n/N (%)	0/1 (0)	0/1 (0)	1/1 (100)
Intra-abdominal, n/N (%)	0/1 (0)	1/1 (100)	0/1 (0)
Bone/joint, n/N (%)	0/1 (0)	0/1 (0)	1/1 (100)