THERAPEUTIC DRUG MONITORING OF CEFTAZIDIME/ AVIBACTAM ADMINISTERED BY CONTINUOUS INFUSION: PK/PD TARGET ACHIEVEMENT AND CLINICAL OUTCOMES

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BACKGROUND AND IMPORTANCE

Ceftazidime/avibactam (CAZ/AVI) ➡ novel β-lactam antibiotic for MDR gram-negative bacteria. Therapeutic drug monitoring (TDM) ensures that CAZ/AVI levels achieve the pharmacokinetic/pharmacodynamic (PK/PD) target. Continuous infusion (CI) has been used to optimize CAZ/AVI pharmacodynamics.

AIM AND OBJECTIVES

To analyze the correlation between PK/PD target attainment of CAZ/AVI administered by CI, clinical outcomes and toxicity.

MATERIALS AND METHODS

Patients treated with CI of CAZ/AVI undergoing TDM of the CAZ plasma concentrations were included. Definitions:

- ✓ **CAZ/AVI PK/PD target:** time that free concentrations remain 4 times above the MIC of the causative pathogen (%fT>4xMIC). (MIC: 8 mg/L assumed if real one not available)
- ✓ **Overexposure**: %fT>10xMIC
- ✓ **Clinical cure:** disappearance of all signs and symptoms related to the infection and no requirement for additional antibiotic treatment (except as part of de-escalation strategy) initiation for the disease to be investigated within 48 h after completion of the study drug
- ✓ **Thirty-day all cause mortality:** death from any cause during the 30 days following the end of treatment

RESULTS

- n:31 patients (28 males, median (range) age of 64 (37-78) years)
- 26 directed treatments (21 XDR-PA and 5 ESBL-K.pneumoniae) and 5 empirical

- ✓ **83.9% (n:26) achieved the PK/PD target** (15 %fT>10xMIC). Only 4 (26.6%) overexposed patients presented adverse reactions (3 increased liver enzymes and 1 thrombocytopenia).
- ✓ **67.7% (n:21) achieved clinical cure**, 18 (85.7%) of which achieved the PK/PD target. Higher frequency of patients with a %fT>4xMIC achieved clinical cure (18/26 (69.2%) in patients with clinical cure vs 2/5 (40%) with clinical failure, p= 0.686).
- ✓ **30-day all-cause mortality: 19.4 % (6 patients).** Lower mortality rate in patients that achieved a %fT>4xMIC (14.8% in patients who survived vs 50% in those who died, p=0.096).

CONCLUSION AND RELEVANCE

CI seems a useful strategy to reach the PK/PD target of CAZ/AVI. Few patients with overexposure presented adverse events. There seems to be a correlation between PK/PD target attainment, clinical cure and 30-day all-cause mortality but larger studies with bigger samples are needed.

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