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1288. Evaluation of Predictors for Clinical Success in Patients Treated with Eravacycline for Various Infections

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Session: P-72. Resistance Mechanisms

Background. Eravacycline (ERV) is approved in the United States (US) for the treatment of complicated intra-abdominal infections in adults. We aimed to evaluate the independent predictors of clinical success in patients treated with ERV for various infections.

Methods. Multicenter, retrospective, observational study conducted from September, 2018 to April, 2021. We included adults treated with ERV for ≥72 hours. Clinical success was defined as 30-day survival, lack of 30-day infection-recurrence, and resolution of infection signs/symptoms. All outcomes were measured from ERV initiation. Multivariable logistic regression (MLR) was performed to identify independent predictors of clinical success. Clinically relevant variables were selected for model entry based on bivariate comparisons (P< 0.2) in a backward fashion.

Results. We included 223 patients from 16 medical centers in 13 geographically unique states. The median (IQR) age was 61 (50-69) years, 57% were male and 62% were Caucasian. Median (IQR) APACHE II and Charlon Comorbidity scores were 15 (10-21), and 3 (1-5), respectively. Sources of infection were primarily intra-abdominal (27%) and respiratory (27%). Common pathogens included Acinetobacter baumannii (21%) and those of the Enterobacteriales order (36%). Infectious diseases consultation and surgical interventions were obtained in 93.7% and 52% respectively. Clinical success occurred in 64%, specifically 30-day survival in 78%, absence of 30-day infection-recurrence in 93%, and 74% experienced resolution of infection signs/symptoms. Since characteristics and outcomes were similar among various pathogens, MLR was conducted using the overall cohort. Skin was a source and combination therapy with ERV were independently associated with higher clinical success: odds ratio 3.3 (CI 1.1-10.2) and 2.9 [1.4-5.9], respectively. Whereas, ICU admission at culture time and undergoing surgery within 30 days of culture were independently associated with reduced odds of clinical success: 0.4 [0.17-0.80] and 0.3 [0.11-0.66] respectively.

Conclusion. Although most ERV treated patients experienced clinical success, factors independently associated with higher clinical success are crucial to consider for optimum antibiotic selection.

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1.290. Ceftazidime-Avibactam Resistance Report in a Third Level Hospital in Mexico City

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Session: P-72. Resistance Mechanisms

Background. The surge of resistant Gram-negative organisms has been worrying infectious disease physicians and physicians in general because of the lack of a large number of antibiotics to which these organisms remain susceptible. Ceftazidime-Avibactam (CAZ-AVI) is a drug approved by the FDA to treat complicated urinary tract infections (cUTI), complicated intra-abdominal infections (cIAIs) in combination with metronidazole, and recently for the treatment of nosocomial pneumonia. Worldwide resistance rates of Enterobacteriaceae to CAZ-AVI have been reported below 2.6%, and 4-8% for Pseudomonas aeruginosa. The FDA, CLSI, and EUCAST assigned the clinical breakpoints of susceptibility: MIC < <=8 mg/liter susceptible, and >>=8/mg/liter, resistant. In Mexico, CAZ-AVI was approved in 2018, and its cost is very high compared to other antimicrobials, so its use is limited in very specific cases. The resistance rates to this antibiotic in the Mexican population remain largely unknown.

Methods. We tested 106 specimens for susceptibility to ceftazidime-avibactam using the disk Kirby-Bauer method. The inhibition zone diameter was determined in mm. Colonial inhibition zone diameters of 21 mm or greater were considered as sensitive, 17-20 mm were considered as intermediate, and <16 mm were resistant.

Results. We found 5 specimens (4.71%) resistant to ceftazidime-avibactam, corresponding to E. coli (3) and P. aeruginosa (2). Two of these were also resistant to colistin, and 4 to meropenem. All carbapenem-resistant isolates harbored Metallo-beta-lactamases genes. For E. coli, NDM gene was held, and for P. aeruginosa the VIM gene (GeneXpert® Cepheid).

Conclusion. The ceftazidime-avibactam resistance among Gram-negative bacteria in our study is similar to the one reported in other international studies. We need more studies in our population to know the nationwide resistance to this antibiotic.

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Methods. PROVE is a multi-center, chart review study of CFDC use for resistant Gram-negative infections (GNI). Cases were eligible if they received ≥ 72 hrs of CFDC. Demographics, comorbidity, pathogen, infection site, and treatment course were assessed. Outcomes included all-cause 14-day and inpatient mortality and length of stay (LOS). Clinical resolution was defined by documentation that clinical signs and/or symptoms had resolved or improved without relapse.

Results. 24 patients who were treated with CFDC at 2 sites were included to date. Median age was 48 years (Range: 19 - 69 years); 33% were female. The most common comorbidity was diabetes (n=7, 29%). Median total ICU LOS was 36 days. Targeted treatment of documented GNI without preceding failure of prior therapy accounted for 71% of CFDC use. Empirical and salvage treatments accounted for 4% and 25% respectively (Table 1). Median time from admission to 1st CFDC dose was 21 days. Acinetobacter baumannii and Pseudomonas aeruginosa accounted for > 75% of isolates (Fig 1). 92% of patients had CR isolates; > 50% were respiratory. Sensitivity to CFDC was tested in 58% of which 71% were sensitive. All-cause 14-day post-CFDC mortality was 13% (95% CI: 2, 27) and overall hospital mortality 25% (95% CI: 6, 44). Clinical resolution was reached in 54% (95% CI: 33, 76). Median post-CFDC LOS was 40 days. Outcomes were stratified by key covariates (Table 2).

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Table 1. CFDC Use Patterns

| Characteristic | N | % |
|---------------|---|---|
| Number of Patients | 24 | 100% |
| Reason for starting ceftazidem | 17 | 71% |
| Empirical for suspected CR GNB | 6 | 25% |
| Adverse drug reactions | 4 | 17% |
| Clinical failure/infection not resolved | 8 | 33% |
| Clinical signs/symptoms resolved | 6 | 25% |
| Patient died | 1 | 4% |
| Switched to alternative susceptible drug(s) | 1 | 4% |

| Days on CFDC | Median (Q1–Q3) | 12.5 (10.5–15) |
|-------------|----------------|-----------------|
| Min-Max     | 7-52           |
| Admission to pos. care | Median (Q1–Q3) | 12 (2.5–36) |
| Min-Max     | 9-256          |
| Positive culture to 1st CFDC dose | Median (Q1–Q3) | 4.5 (2–8) |
| Min-Max     | 5-18           |

| Antibiotics in use before CFDC | N | % |
|-------------------------------|---|---|
| Cefazolin                      | 2 | 10% |
| Ceftazime                      | 1 | 5% |
| Ceftazidime-Avibactam          | 1 | 5% |
| Ceftiraxone                    | 1 | 5% |
| Ceftarol                      | 1 | 5% |
| Meropenem                     | 8 | 33% |
| Minocycline                   | 1 | 5% |
| Piperacillin/Tazobactam        | 5 | 25% |
| Tigecycline                    | 2 | 10% |

| Antibiotics added on CFDC (concurrent, combo therapy) | N | % |
|------------------------------------------------------|---|---|
| Amphocilin                                         | 1 | 3% |
| Ampicillin/Amoxicillin/Smeltobactam                 | 1 | 3% |
| Ceftazidime-Avibactam                              | 1 | 3% |
| Imipenem                                           | 3 | 13% |
| Imipenem-Relebaactam                                | 1 | 3% |
| LEVETIRACONON                                    | 1 | 3% |
| Meropenem                                          | 5 | 13% |
| Minocycline                                        | 1 | 3% |
| Piperacillin/Tazobactam                            | 2 | 7% |

[1] Antibiotics used for at least 2 days with start date on or before ceftazidem initiation date.

Table 2. Outcomes by Key Covariates

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