Patients Treated With Aztreonam and Ceftazidime

2409. Drug-Induced Liver Injury (DILI) in a National Cohort of Hospitalized Patients Treated With Aztreonam and Ceftazidime
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Background. DILI, although uncommon, can be a severe and even fatal complication of antibiotic use. The safety of novel regimens targeting MDR Gram-negative bacteria (GNB) is an important concern. Cephalosporins such as ceftazidime (CAZ) are rare causes of clinically apparent DILI, while data regarding DILI with other antibiotics such as the monobactam atorvastatin (ATM) are sparse. ATM and CAZ are partnered with many novel β-lactamase inhibitors (i.e., avibactam, AVI) as therapy for MDR infections (CAZ-AVI and ATM-AVI). We aimed to compare the incidence and type of DILI associated with ATM and CAZ.

Methods. Using a cohort of patients hospitalized within Veterans Health Administration (VHA), we identified patients treated with ATM or CAZ for 3 or more consecutive days who also had LFT measurements during (day 3 or later) or within 7 days of stopping treatment. We excluded patients with abnormal LFTs in the year prior to ATM or CAZ treatment. Using alamine aminotransferase, alkaline phosphatase, and bilirubin measurements, we applied clinical chemistry criteria to identify cases of DILI. We applied further criteria to classify DILI according to clinical pattern and severity (mild vs. moderate/severe), comparing the relative frequencies between ATM and CAZ.

Results. Among 18,813 courses of CAZ or ATM, 3,432 ATM and 2,662 CAZ courses met our criteria (Figure 1). While the overall rate of any DILI was higher in ATM than CAZ (5.8% vs. 3.2%, P < 0.01), the rate of moderate/severe DILI was similarly low for both agents (1.6% in ATM vs. 1.3% in CAZ, P = 0.5). The clinical pattern of DILI cases differed by drug, with the hepatocellular pattern comprising a larger proportion of the ATM DILI cases (37%) than the CAZ DILI cases (25%) and the cholestatic pattern comprising a smaller proportion (48% vs. 61%) (Figure 2).

Conclusion. The delay in appropriate antimicrobial therapy did not affect the clinical outcome of patients if they were properly treated thereafter. This suggests that prescription of a broad-spectrum antibiotics was not needed as initial empirical antibiotics for the treatment of APN with a potential risk of EBSL-PE.

Figure 1. Time to recurrence within 1 year after initial APN episodes.

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2410. Clinical Outcomes Associated With Various Treatment Options for Infections Caused By Carbapenem-Resistant Enterobacteriaceae
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Background. Infections caused by carbapenem-resistant Enterobacteriaceae (CRE) have been designated an urgent level threat to public health. With the advent of novel β lactam/β-lactamase inhibitor combinations, the armamentarium against CRE is expanding. Our study aims to evaluate clinical outcomes in patients with CRE infections.

Methods. A retrospective study was conducted to compare clinical outcomes in adult patients with documented CRE infections between January 2009 and December 2017. Infections caused by carbapenem-resistant Enterobacteriaceae (CAZ-AVI) were included in this study. All patients with CRE infections were treated with either carbapenem-based (BAT) or colistin-based (CMB) regimen. The following clinical outcomes were assessed: clinical cure, total length of stay (LOS), 30-day mortality, and infection-related mortality.

Results. One hundred and fifty patients met criteria for inclusion; 25 in the CAZ-AVI group and 125 in the BAT group. The median Charlson Comorbidity Index (CCI) was 6 in both cohorts, indicating a low baseline probability for survival. The most common primary sites of infection for the CAZ-AVI and BAT cohorts, respectively, were the following: blood (24% vs. 18%, P = 0.580), urinary tract (36% vs. 23%, P = 0.209), intraabdominal (16% vs. 14%, P = 0.754), and lung (12% vs. 27%, P = 0.132). Combination therapy was utilized in 8% of patients in the CAZ-AVI group compared with 42% in the BAT group. There were statistically significant differences in the frequency of antibiotics used and in the frequency of appropriate empirical antibiotics.

Conclusion. In this national cohort of hospitalized patients treated with ATM or CAZ, the overall rate of DILI was significantly higher in patients treated with ATM than in those treated with CAZ. However, there is a similarly low rate of moderate/severe DILI. Although further analyses are required to better understand causal mechanisms and clinical risks of DILI in patients receiving ATM or CAZ, these data from a large national cohort provide a useful benchmark of drug safety.

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statistically significant difference in both all-cause mortality (24% vs. 73%, P = 0.006) and infection related mortality (4% vs. 26%, P = 0.017) in the CAZ-AVI and BAT groups, respectively. There was a trend toward a lower overall length of stay favoring the CAZ-AVI cohort as opposed to the BAT cohort (16 days vs. 30 days, P = 0.082).

**Conclusion.** CAZ-AVI therapy was associated with lower mortality rates for CRE infections and have a high attributable mortality, especially with concomitant bactemia. Future studies are warranted to confirm these results.

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**2411. Expanded Susceptibility and Resistance Mechanism Testing Among Carbapenem-Resistant Enterobacteriaceae in Connecticut, 2017**

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**Background.** In Connecticut (CT), submission of clinical carbapenem-resistant Enterobacteriaceae (CRE, resistant to ≥1 carbapenem) isolates to the state public health laboratory (SPHL) was mandated in 2017 for expanded susceptibility and carbapenemase testing. To guide empiric treatment, we created a statewide CRE antibiogram and explored the role of carbapenemase production.

**Methods.** Susceptibility testing was conducted by broth microdilution and disk diffusion and interpreted using Clinical and Laboratory Standards Institute (CLSI) breakpoints, if available. Carbapenemase-producing CRE (CP-CRE) were identified using the modified carbapenem inactivation method (mCIM). Multiplex real-time polymerase chain reaction testing was used to identify genes for common carbapenemases.

**Results.** Of 198 CRE isolates received by the SPHL in 2017, 166 were confirmed as CRE. After patient deduplication, 147 records remained (46.9% of patients). CRE were identified using the modified carbapenem inactivation method (mCIM). Multiplex real-time polymerase chain reaction testing was used to identify genes for common carbapenemases.

**Conclusion.** CP-CRE have demonstrated significant resistance to non-carbapenem antibiotic classes. Most CRE isolates were susceptible to CAZ-AVI and colistin. The predominant carbapenemase gene is blabimex. This statewide antibiogram can guide empirical prescribing and formulary selection for CRE treatment.

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**2413. The Role of Minocycline in the Treatment of Nosocomial Infections Caused by Multidrug, Extensively Drug and Pandrug-Resistant Acinetobacter baumannii: A Systematic Review of Clinical Evidence**

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**Background.** Treatment options for multi-drug-resistant (including extensively and pandrug-resistant) Acinetobacter baumannii strains (herein MDR-AB) are limited. Minocycline, a synthetic tetracycline derivative, has been used alone or in combination in the treatment of infections associated with AB. We systematically reviewed the available clinical evidence regarding its role in the treatment of nosocomial infections caused by MDR-AB isolates in adult patients.

**Methods.** A systematic review of the published literature examining the clinical use of minocycline in nosocomial infections associated with MDR-AB isolates (defined according to ECDC guidance) was performed according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) Guidelines. PubMed, Scopus and Web of Sciences databases were searched from their inception until the March 20, 2018. Three researchers individually evaluated the available clinical studies according to predefined inclusion and exclusion criteria. No language restrictions were applied.

**Results.** 27 patients received IV fosfomycin. Of these 6 were excluded from the study because 2 had SIRS due to non-infective etiology, 1 had an organism with Fosfomycin resistance and 3 had incomplete clinical records. 7 patients received empirical and 14 received directed treatment. The most frequent isolate was carbapenem-resistant Klebsiella pneumoniae found in 8 patients. 1 patient received monotherapy while 20 received combination therapy: 9 patients were clinically cured. 1 showed clinical improvement, 8 worsened on treatment due to adverse drug reactions and 3 patients died while on treatment. Microbiological cure was seen in 6 patients. 3 had persistently positive cultures. 1 patient with bacteremic UTI due to Klebsiella pneumoniae received IV fosfomycin for 14 days and relapsed after 1 week of stopping treatment with the same organism showing fosfomycin resistance. 16 patients developed adverse drug reactions. The most common adverse drug reaction was diarrhea in 13, among them 1 had C. difficile colitis. Other adverse reactions like hypernatremia and hypokalemia were observed in 7 and 10 patients, respectively. Electrolyte imbalance were seen in patients aged >50 and those who received a higher dose than was appropriate for the creatinine clearance. 2 patients developed noncardiogenic pulmonary edema within 72 hours of starting fosfomycin and 1 developed torsades de pointes with QT prolongation due to hypokalemia.

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