2258. Correlation of Electroencephalogram Findings and Dose Relative to Renal Function among Patients with Possible Cefepime-Induced Encephalopathy

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Background. Cefepime-induced encephalopathy (CIE) is thought to be a rare toxicity with an overall incidence of <1%. However, the low incidence may be a result of under-recognition and difficulty in identifying the exact etiology of encephalopathy in hospitalized patients. Among patients with suspected CIE, electroencephalograms (EEGs) sometimes show abnormal activity like triphasic waveforms (TPWs). We asked whether the incidence of EEG findings consistent with CIE varies with cefepime (CFP) dose relative to eGFR (dose/eGFR). We also compared the incidence of these EEG findings in patients receiving CFP to the incidence in patients receiving piperacillin-tazobactam (PT).

Methods. In a retrospective analysis, data between 8/1/2016 and 5/24/2018 were extracted from the University of Chicago Clinical Data Warehouse. Patients 20–79 years old who received PT or CFP were included; those requiring renal replacement therapy or who had eGFR <10 mL/minute/BSA at baseline were excluded. The average daily dose of PT or CFP was calculated to determine dose/eGFR. Linear or logistic regressions were performed in STATA.

Results. EEGs were obtained in 66 (4.3%) of 1525 patients receiving CFP and in 28 (3.3%) of 842 receiving PT. TPWs were present in 19 (28%) of EEGs from the CFP group, and in none of the EEGs from the PT group. Figure 1 shows the correlation between CFP dose/eGFR ratio and occurrence/severity of TPWs. Ordered logistic regression analysis identified a coefficient of 20.9 (95% CI: 3.7–38.2). Figure 2 shows only a weak association between CFP dose/eGFR and background frequency (BFS; R² = 0.05). In the PT group, BFS was not correlated with PT dose/eGFR (R² = 0.01). TPWs were more likely to be found in patients receiving CFP than PT, suggesting that in the absence of other metabolic abnormalities, TPWs might be specific for CFP. Higher CFP dose-to-eGFR ratios predispose to and potentially worsen the severity of TPWs. Unlike TPWs, BFS was only weakly associated with PT dose/eGFR ratio and even less associated with PT dose/eGFR ratio.

Disclosures. All authors: No reported disclosures.

2259. Predictors of Empiric Carbapenem Therapy in Complicated Intra-Abdominal Infections in the United States, 2013–2017: A Retrospective Cohort Study

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Background. Complicated intra-abdominal infections (cIAI) remain an important cause for hospitalization. Evidence-based guidelines recommend reserving broad-spectrum antibiotic coverage for high-risk cases in order to reduce overuse of certain antibiotic classes, particularly in the face of emerging carbapenem resistance. We examined the factors associated with use of empiric carbapenem treatment (ECT) among hospitalized patients with cIAI.

Methods. We performed a multicenter retrospective cohort study in the Premier database of approximately 180 hospitals, 2013–2017. Using an ICD-9/10 based algorithm including a requirement for a laparotomy/laparoscopy, we identified all adult patients hospitalized with cIAI and included those with a positive blood or abdominal culture. We derived and tested a multivariable logistic regression model to examine predictors of ECT.

Results. Among 321,317 hospitalized patients with cIAI, 4,453 (1.4%) were culture-positive, 1,185 (26.6%) of whom received ECT. Among those given ECT, >50% (682) had no risk factors for resistance, and in only 120 (10.1%) was an organism resistant to a third-generation cephalosporin (C3R extended spectrum β-lactamase [ESBL] phenotype) isolated. The top 5 variables associated with ECT use were: pre-cIAI anti-fungal therapy (OR 2.57, 95% CI 1.91, 3.45) urgent (vs. emergent) admission (OR 1.56, 95% CI 1.21, 2.01), corticosteroids (OR 1.50, 95% CI 1.13, 1.99), ICU admission (OR 1.46, 95% CI 1.17, 1.82), and presence of sepsis/septic shock (OR 1.43, 95% CI 1.18, 1.74). The model had a moderately good fit (c-statistic = 0.683; 95% CI 0.665, 0.700). Hosmer-Lemeshow P value = 0.411.

Conclusion. Among patients hospitalized with a cIAI, 26.6% received ECT despite >50% lacking risk factors for resistance, and an only 10% prevalence of C3R in this cohort. This suggests that there remains an opportunity for carbapenem-sparing strategies. Further stratification of the risk for resistance is needed among patients with markers of high illness severity, such as those identified in our model.

Disclosures. All authors: No reported disclosures.

2260. Clofazimine Safety and Efficacy for Treatment of Multidrug-Resistant Non-Tuberculous Mycobacteria (NTM)

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Background. Nontuberculous mycobacteria (NTM) are increasingly detected in patients with chronic pulmonary or extrapulmonary NTM infection among those treated with clofazimine and led to clinical improvement in the majority of those treated. Randomized controlled studies are needed to determine the individual impact of clofazimine within and otherwise optimized regimen.

Methods. A prospective cohort study was performed in patients diagnosed with pulmonary or extrapulmonary NTM infection among those treated with clofazimine from a single center serving referrals from across the state of Virginia under an investigational new drug protocol. Data were collected through the center's electronic medical record and included both pretreatment and follow-up host characteristics, radiological, microbiological and pathology data. Outcomes were assessed, radiological resolution, symptom improvement, and change in pulmonary function test (among patients with cystic fibrosis).

Results. Thirty-seven patients received clofazimine. NTM species for which the treatment was indicated were M. abscessus in 21 (58%), M. avium complex in 17 (45%) and 3 with M. chelonae. The most common companion drugs for M. abscessus included imipenem, tigecycline, linezolid or tazobactam, amikacin (IV induction followed by inhale combination phase) and ampicillin. For other basic patient characteristics refer to Table 1. Survival rate was 97%, while 73.5% had documented improvement in symptoms and only 2.9% had worsening of symptoms. Radiological resolution or partially improving were documented in 38% of the patients. There were no severe adverse events from clofazimine.

Conclusion. Adding clofazimine to multi-class antibiotic regimens for drug-resistant NTM treatment, including pulmonary M. abscessus disease, was well tolerated and led to clinical improvement in the majority of those treated. Randomized controlled studies are needed to determine the individual impact of clofazimine within and otherwise optimized regimen.

Disclosures. All authors: No reported disclosures.
2261. Oral Fosfomycin for Treatment of Urinary Tract Infections Due to Extended-Spectrum β-Lactamase and Carbapenem-Resistant Enterobacteriaceae

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Background. Urinary tract infections (UTIs) caused by extended spectrum β-lactamase (ESBL) and carbapenem-resistant Enterobacteriaceae (CRE) pose a significant challenge due to limited treatment options. The objective of this study was to compare outcomes in patients treated with standard IV therapy or oral fosfomycin for ESBL and CRE UTIs.

Methods. Retrospective cohort review of inpatients diagnosed with ESBL and CRE UTIs between June 2016 and September 2017 at a seven-hospital system. Patients with polymicrobial UTI, bloodstream infections, additional anatomic site with ESBL/CRE, or those requiring renal replacement therapy were excluded. Only patients with documented fosfomycin susceptible isolates in vitro were included. Eligible patients were divided into two groups: standard IV therapy (SDTx) or fosfomycin therapy (FOS). FOS group could receive ≤72 hours of other active antibiotics from urine culture collection (UTI onset) to the first dose of fosfomycin. Quick sequential organ failure assessment (qSOFA) scores were calculated at UTI onset. The primary endpoint was functional cure defined as resolution of symptoms without microbiological failure. Microbiological failure was defined as a positive urine culture within the index hospitalization or 30 days.

Results. There were 70 patients included: 31 treated with SDTx and 39 with FOS. ESBL Echerichia coli was most common, accounting for 58% of UTIs in SDTx and 71.8% in FOS. ESBLs accounted for 71% (n = 22/31) of UTIs in SDTx and 89.7% (n = 25/31) in FOS. The overall qSOFA score was 0.7 (range, 0–3) with the majority of patients scoring ≤2 (80.6% in SDTx vs. 92.3% in FOS; P = 0.29). There was no significant difference in functional cure rate (n = 30, 96.8% SDTx vs. n = 37, 94.9% FOS; P = 0.83). SDTx patients had a longer length of stay (15.3 days vs. 7.3 days with FOS; P = 0.04), duration of active therapy (7.6 days vs. 3 days with FOS; P < 0.0001), and time from UTI onset to discharge (10.3 days vs. 6.6 days with FOS; P = 0.002). There were no adverse drug events reported.

Conclusion. Oral fosfomycin was a safe and effective alternative to standard IV therapy for ESBL and CRE UTIs in this investigation and demonstrated similar functional cure rates. Additionally, patients treated with fosfomycin had shorter hospitalizations and durations of antibiotic therapy.

Disclosures. All authors: No reported disclosures.

2262. Ceftazidime–Avibactam vs. Polymyxin B in the Treatment of Infections Due to Carbapenem-Resistant Enterobacteriaceae

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Background. Pharmacotherapy for carbapenem-resistant Enterobacteriaceae (CRE) infections is limited. There is a paucity of evidence to guide optimal management of CRE infections. Ceftazidime–avibactam, a novel cephalosporin–β-lactamase inhibitor, may be a reasonable alternative to colistin for CRE infections, but data on polymyxin B (PB) are lacking. Given the improved pharmacokinetic profile of PB compared with colistin, we sought to evaluate clinical and microbiological outcomes of patients treated with CAZ-AVI or PB for CRE infections.

Methods. We conducted retrospective cohort study in adult patients treated with CAZ-AVI or PB for a CRE infection between June 2010 and August 2018. The primary outcome was all-cause mortality at 30 days. Secondary outcomes included clinical cure, microbiological cure, and development of resistance. Endpoints were analyzed using standard statistical measures. The influence of clinical variables other than antimicrobial therapy was assessed in a multivariable regression analysis.

Results. The study included 117 patients, with 42 patients receiving CAZ-AVI and 75 receiving PB. Respiratory and urinary tract infections were most common, occurring in 37.6% and 20.5% of patients, respectively. Bloodstream infections occurred in 45 (35.9%) patients. In the CAZ-AVI group, there were 9 deaths (21.4%), compared with 19 deaths (25.3%) in the PB group (P = 0.653). No statistically significant differences were found in clinical cure or microbiologic cure between CAZ-AVI and PB. PB was associated with a higher incidence of nephrotoxicity (19% vs. 43%; P = 0.048). After adjustment for duration of therapy, combination therapy, and initial WBC, use of PB was not an independent predictor of mortality.

Conclusion. No statistically significant differences between CAZ-AVI and PB were found in clinical or microbiologic outcomes in this cohort of patients treated for CRE infection. Further studies are necessary to confirm these preliminary findings to optimize clinical practice.

Disclosures. All authors: No reported disclosures.

2263. Fosfomycin Tapered Use for Complicated UTIs Including Pyelonephritis, a 1-year Review of Outcomes and Prescribing Habits

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Background. Treatment of complicated urinary tract infections (UTI) caused by multidrug-resistant organisms (MDROs) is increasingly problematic given limited oral antibiotic options. In these situations, fosfomycin is increasingly used. However, there are limited outcome and pharmacokinetic data to support fosfomycin use for complicated UTIs (cUTI), especially in the upper tract. We describe fosfomycin use for complicated cUTI in our healthcare system.

Methods. We performed a retrospective review of all fosfomycin prescriptions between 1/1-December 31/17 in the Los Angeles Department of Health Service system, which consists of 4 medical centers and 19 clinics that provide care to >600,000 patients annually. In our system, fosfomycin use requires ID approval. We collected demographics, clinical characteristics, adverse effects, and 30-day success.