were performed in duplicate using C/T free concentrations reflective of the peak and trough of a 3g q6h dose (120/25.2 μg/mL, 7.5/1.66 μg/mL) and the peak of a 1.5g q8h dose (60/12.6 μg/mL) in humans. The activity of C/T 120, 60, and 7.5 alone and C/T 7.5 in combination with free peak concentrations of FEP, CIP, CST, ATM, MEM, TZP, FOF, or AMK was tested for all isolates. Colony counts were determined at 0, 3, 6, and 24h by serial dilution plating. Synergy was defined at ≥2 log₉ CFU reduction from the most active agent.

Results. MICs of the 4 MDR P. aeruginosa isolates are in Table 1. As the C/T concentrations increased, bacterial reduction improved, achieving a mean (±SD) log₉ CFU change from 0 h of 0.03 (0.07), −1.19 (1.03), −2.59 (0.86) with C/T 7.5, 60, 120, respectively. C/T 7.5 was synergistic with CST (PSA C21-31, PSA C45-10) and FOF (PSA C28-5, PSA C14-22) in two of four isolates. No synergy was observed with double β-lactam therapy or CIP. AMK alone achieved maximal bacterial kill; therefore, synergy could not be assessed.

Conclusion. C/T 3g and 1.5g q6h peak concentrations demonstrate killing against the MDR PSA. CST and FOF were synergistic with C/T in vitro. Our findings aide in identification of novel treatment options and dosing regimens for the treatment of MDR P. aeruginosa.

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835. Impact of an Extended Infusion B-lactam Strategy on Outcomes in Critically Ill Patients with Pseudomonas Infections

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Session: 77. Use of PK/PD to optimize existing antibiotics and antifungals

Thursday, October 5, 2017: 12:30 PM

836. Influence of Polymyxin B Dose on Development and Recovery of Acute Kidney Injury

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837. Assessing the Risk of Nephrotoxicity Associated With Non-renally Adjusted Intravenous Polymyxin B Compared With Traditional Dosing

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**Background.** Prior data states that polymyxin B is renally cleared and thus required renal adjustments, however newer data suggests that polymyxin B undergoes non-renal clearance. With more aggressive dosing, potential for increased nephrotoxicity is of concern. This study aims to determine what time to acute kidney injury (AKI) differs between renally adjusted and non-adjusted doses of intravenous (IV) polymyxin B. Secondary objectives aim to evaluate incidence of AKI, length of stay (LOS), adverse reactions, and potential role of ascorbic acid in decreasing nephrotoxicity.

**Methods.** This retrospective chart review compared time to AKI in patients receiving renally adjusted and non-adjusted IV polymyxin B between Jan 2012 and Nov 2016. This study included patients who are at least 18 years old, received IV polymyxin B, and have creatinine clearance below 80 mL/minute. Patients were excluded if they had AKI (RIFLE criteria), received renal replacement therapy, or are pregnant prior to receipt of IV polymyxin B. Fine and Gray's model for competing risks was used to predict the cumulative incidence function of AKI. Descriptive statistics, two-sample t-test, and Chi-square test were used as appropriate.

**Results.** Of the 132 patients screened, 54 met inclusion criteria (23 in the renally adjusted vs. 31 in the non-adjusted group). There was no statistical association between dosing type and time to AKI (P = 0.13). Incidence of nephrotoxicity was higher in the renally adjusted vs. non-adjusted groups (21.7% vs. 6.5% respectively). Mortality was higher in the renally adjusted vs. non-adjusted groups (17.4% vs. 6.5% respectively). LOS was greater in the renally adjusted vs. non-adjusted groups (16 vs. 14 days respectively, P = 0.06). All patients in the study received concomitant nephrotoxic agents (e.g., vancomycin, aminoglycosides). Ascorbic acid use was infrequent but, in the 4 patients who did receive it, none developed AKI. No difference in neurotoxicity, respiratory arrest, Clostridium difficile infections was seen.

**Conclusion.** No significant association between IV polymyxin B dosing type and time to AKI was found. Incidence of AKI, LOS, and mortality was higher in the renally adjusted group compared with the non-adjusted group. Ascorbic acid may mitigate the nephrotoxic potential of IV polymyxin B, but further studies are needed.

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