O241
Oral Session
New old antibiotics: safety and efficacy

COLISTIN-ASSOCIATED NEPHROTOXICITY IN CRITICALLY ILL PATIENTS AND SIMULATED COLISTIMETHATE SODIUM AND COLISTIN LEVELS

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Objectives: This study investigates risk factors for nephrotoxicity (NTX) associated with colistin (administered as intravenous [IV] prodrug colistimethate sodium [CMS]) in a critically ill patient population.

Methods: A retrospective cohort of adult patients treated with colistin at Jackson Memorial Hospital (Miami, FL) from January 2008 through November 2010 was evaluated. Exclusion criteria included serum creatinine (SCr) >2 mg/dL or renal replacement therapy on day 1 of colistin therapy, history of kidney transplantation, <72 hours therapy, and initiation of colistin outside an intensive care unit (ICU). NTX was defined as at least two consecutive SCr measurements with an increase of 0.5 mg/dL from baseline at least 24 hours apart after two or more days of therapy. RIFLE criteria were used to assess acute kidney injury. A population pharmacokinetic model was run to simulate CMS and colistin concentrations. Non-compartmental analysis (NCA) was performed to obtain estimates of total treatment area under the curve (AUC), maximum concentration (Cmax), and minimum concentration (Cmin) values. NCA results were used with demographic and clinical data in a binary analysis to screen for variables related to NTX. All p-values <0.3 were entered into a hierarchical forward stepping with replacement logistic regression algorithm.

Results: 112 patients met inclusion criteria. 65% of patients were male, the median age was 47.9 years, 46% of patients were in a surgical ICU and the median APACHE II score was 17.2. Simulations produced mean colistin Cmin and Cmax values of 0.93 mg/L and 1.3 mg/L, respectively. 39% of patients experienced NTX with 11%, 27% and 61% in the risk, injury and failure categories, respectively. There was a median of 5.5 days to NTX onset. The bivariate analysis identified NTX risk factors of actual body weight, ideal body weight, body mass index (BMI), age in years, diabetes, concomitant IV contrast, beginning SCr, beginning CrCl, and for both colistin and CMS, cumulative AUC, daily AUC, Cmax and Cmin. The logistic regression analysis based upon Cmax and Cmin values identified independent risk factors for colistin-associated NTX of BMI >31.5 kg/m^2 (OR 2.0, 95% confidence interval [CI] 0.9-4.6), age (OR 1.05, 95% CI 0.99-1.1), IV contrast (OR 4.9, 95% CI 2.1-11.7), and colistin Cmax (OR 13.7, 95% CI 4.1-46). 41% and 24% of patients died by day 30 in the NTX and non-NTX groups, respectively (p=0.08).

Conclusion: A dosing strategy minimizing colistin Cmax (e.g., prolonged infusions) and avoidance of IV contrast along with therapeutic drug monitoring of colistin concentrations may be useful in avoiding and/or reducing colistin-associated NTX.