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**Background**

CMS has re-emerged as a treatment option in patients infected with MDR GNB. The extent to which PK/PD of colistin is correlated with clinical outcomes of the patients treated with CMS is limited. The objectives of the study were to determine PK and PD of colistin, and outcomes of the patients infected with MDR GNB who were treated with CMS.

**Methods**

This is an ongoing study entitled “Optimizing dosing of colistin for infections resistant to all other antibiotics” supported by NIAID/NIH (R01-AI70896-01). 103 Thai patients aged ≥ 18 years with pneumonia or bloodstream infection due to GNB resistant to beta-lactams, fluoroquinolones and aminoglycosides who received CMS from January 2009 to August 2010 were included. Blood samples for PK study were collected on day 3 - 4 of CMS therapy. CMS and formed colistin concentrations in plasma were quantified by HPLC. MICs of colistin against all isolates of MDR GNB were determined by broth microdilution and Etest. All patients were followed up to day 90 after CMS therapy.

**Results**

Of 103 enrolled patients, 89 (86%) did not receive renal replacement therapy. 57% were males. Median age of the patients was 72 years (range 18 – 92). Median body weight was 55 kg (range 30 – 122). 91% had pneumonia. Median APACHE II score was 21 (range 4 – 38). Median serum creatinine was 1 mg/dL (range 0.3 – 10.5). Median creatinine clearance was 41 mL/min (range 4 to 226). MDR GNB isolates were *A.baumannii* (92%) and *P.aeruginosa* (8%). MIC₅₀ and MIC₉₀ of colistin against MDR GNB were 0.75 and 2 mg/L, respectively (MIC range 0.25 – 4). Median dose of CMS equivalent to colistin base activity was 150 mg/d (range 50 – 300). 93% received combination of CMS and other antibiotics. Median duration of CMS therapy was 13
days (range 3 - 27). Observed PK parameters of colistin: median C_{max} was 2.6 mg/L (range 0.6 - 9.8), median AUC_{0-24} was 54 h.mg/L (range 12 – 196). Observed PD parameters of colistin: median AUC_{0-24}/MIC was 72 (range 9 - 392), median C_{max}/MIC was 3.5 (range 0.4 - 19.6) and median %T>MIC was 100 (range 0 – 100). Cumulative mortality rates were 19%, 37% and 58% at day 14, 28 and 90, respectively. 57% of the mortality was likely or possibly due to the index infection. 38% developed doubling of serum creatinine during CMS therapy. Suggested dosing of CMS to achieve the desired ‘target’ concentrations of colistin in plasma was derived.

Conclusion
CMS is moderately effective for therapy of MDR GNB infections. Traditional CMS doses are often too low in many patients. Favorable clinical outcomes of MDR GNB infections treated with CMS could be improved by providing optimum doses of CMS according to appropriate PK/PD targets.