1404. A Pharmacokinetic Study on CMS and Colistin and Its Impact on Clinical Cure and Acute Kidney Injury in Critically Ill Patients with Normal Renal Function from South India
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Background. Colistin has re-emerged as last line antimicrobial to combat MDR GNB. There is need for robust pharmacokinetic (PK) and pharmacodynamics (PD) data to guide dosing. This study assessed the PK of CMS and colistin and its impact on clinical cure (CC) and acute kidney injury (AKI) in critically ill patients with normal baseline renal function.
Methods. Adult critically ill patients with colistin susceptible MDR/XDR infec-
tions and normal renal function who were treated with intravenous CMS (9MU CMS loading dose (LD) followed by maintenance (MD) 3MU every 8 hour starting 24 hours after LD were recruited into this prospective observational study. For PK sampling, 3ML venous blood was drawn immediately before LD and at 0.5, 1, 2, 4, and 12 hours after LD. During MD, samples were collected before and at 1, 2 and 8 hours after the eighth and ninth infusion. Colistin plasma concentrations were determined by LC–MS. Results. A total of 280 pair serum samples were analysed from 20 patients. Ninety percent had pneumonia. Predominant pathogens were Klebsiella pneumonia (12) and Acinetobacter spp. (8). Mean creatinine clearance (CrCl) was 115 ± 24 mL/minute (72.3–208.8). All patients received combination therapy with colistin, 101 ± 13% of target meropenem and 52% (5/10) received tigecycline. Clinical cure rate was 50% (10/20) and mortality rate was 52% (10/20). Mean LD colistin Cmax were 3 ± 1.1 mg/L (1.75–5.14) and 2.37 ± 1.2 mg/L (1.52–5.54) among CC and CF groups, respectively (P = 0.13). MD colistin Cavg was 2.25 ± 1.3 mg/L and 1.78 ± 1.1 mg/L in CC and CF groups, respectively. The mean AUCC0–t/MIC ratio of MD colistin was 92.76 ± 65.75 and 59.5 ± 12.8 mg/L for CC and CF groups, respectively (P = 0.27). In pneumonia, AUCC0–t/MIC for Acinetobacter spp. was higher in the CC (71.18 ± 10.20) than in the CF group (40.88 ± 16.28) (P = 0.05). Renal injury was noted in 20% and 40% at end of therapy. Ten to 20% of patients with CrCl< 100 mL/minute had Cavg ≥ 2 mg/L. Majority of CF with AKI had Cavg between 1 and 1.5 mg/L.
Conclusion. Clinical cure was low at 50%. Sub-inhibitory Cavg and increased volume of distribution following MD could have contributed to high failure. Colistin exposures were similar to those reported in other published cohorts with no consistent exposure response relationship. Based on these results, there is an important role for therapeutic drug monitoring with Colistin.
Disclosures. All authors: No reported disclosures.