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ePoster Viewing

Antimicrobials: antimicrobial PK/PD, pharmacogenomics, pharmacoeconomics and general pharmacology, drug interaction studies

Urinary concentrations of colistimethate sodium (CMS) and formed colistin in patients with MDR Gram-negative bacterial (MDR-GNB) infections after intravenous administration

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Objectives: Colistin is widely used for treatment of urinary tract infections (UTIs) caused by MDR-GNB; however, little information is available on its urinary excretion in infected patients. This study aimed to investigate the pharmacokinetics of CMS and formed colistin in urine in patients with MDR-GNB infections.

Methods: Pharmacokinetic study was conducted in 9 patients with MDR-GNB infections treated with CMS in a university hospital 1/2014 to 8/2014. Demographics, CMS dose (selected by the physician), estimated glomerular filtration rate (GFR) at start and end of CMS therapy, concentration of CMS and formed colistin in urine, volume of urine, and co-administered nephrotoxic drugs were recorded. A urine sample was collected in each patient prior to CMS administration and over 0-2, 2-4 and 4-6 h. Blood samples were obtained pre-dose ($Cmin_{ss}$) and end of infusion ($Cmax_{ss}$) at steady state for measurement of concentrations of CMS and formed colistin using HPLC. CMS urinary recovery was determined as the summed amount of CMS and formed colistin recovered in urine for each 2-h interval divided by the CMS dose. Quantitative variables were expressed as median (interquartile range) and Spearman test was employed for bivariate correlations.

Results: In the enrolled 9 patients: 7 (77.8%) male, age: 65 (63-70) years; $Cmin_{ss}$ and $Cmax_{ss}$ of CMS in plasma: 4.1 (1.9-4.6) and 10.4 (4.7-11.7) mg/L, respectively; eight patients (88.9%) received nephrotoxic drugs (7 furosemide and 3 vancomycin, being the most common). Clinical and PK data are shown in the Table.

Pt.	CMS dose	Initial/Final GFR (mL/min)*	Colistin $Cmin_{ss}$ (mg/L)	Range of conc. in urine (mg/L) Colistin	Range of conc. in urine (mg/L CMS	CMS Urinary Recovery (%) 0-2h/2-4h/4-6h (total 6h)
1	1MUI/24h	9/7	0.8	0.5-1.7	3.2-18.9	0.9/1.9/0.0 (2.9)**
2	1MUI/8h	266/156	1.5	<0.1-0.6	1.5-64.8	21.0/3.6/0.6 (25.3)
3	1MIU/8h	56/52	0.4	3.2-12.5	37.3-139.2	21.4/20.9/5.3 (47.6)
4	2MUI/12h	49/56	0.9	1.8-4.8	11.1-67.3	7.3/5.4/3.8 (16.6)
5	2MIU/8h	85/108	1.4	9.3-25.9	105.4-362	24.8/7.8/10.0 (42.6)
6	2MIU/8h	93/38	0.8	4.5-15.8	58-211.3	1.2/1.5/18.1 (20.9)
7	3MIU/8h	190/332	0.7	1.9-23.9	78.3-491.4	46.7/1.4/1.3 (49.4)
8	3MUI/8h	122/58	0.9	8.5-21.3	58.7-194.1	29.9/10.9/8.3 (49.0)
9	4.5MIU/12h	136/114	1.4	3.2-95.4	9.2-1699.6	0.2/36.6/40.8 (72.8)

*MDRD-4 equation; **Collected in 4h

In 5 patients, >40% of the CMS dose was recovered in the urine in the first 6 hours. CMS urinary recovery 0-6h showed a tendency with the initial GFR (rho:0.633; p:0.067).

Conclusions: This is the first study to examine the urinary recovery of CMS in patients with a 2-h interval. Concentrations of formed colistin were higher than those in plasma and also above of the MIC value (0.5mg /L) of the predominant strain of *Pseudomonas aeruginosa* in our hospital. Future studies are warranted for optimising CMS dosage regimens in UTI patients.