Is there a need to monitor colistin exposure in critically ill patients?

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Background: Colistin is widely used to treat gram negative infections caused by carbapenem resistant organisms and is known to cause nephrotoxicity and neurotoxicity. This study describes colistin exposure and explores its association with the clinical outcome.

Method: An observational study was performed in 41 critically ill patients who received colistin for culture proven gram negative infections. From an already existing arterial line, 6 to 9 blood specimens were collected in one inter-dose interval between day 2 to day 15, after a loading dose of colistin. Sequential organ failure assessment (SOFA) score was measured on the day of estimation of colistin exposure (DOE), day 3 and day 7 of colistin therapy. Acute kidney injury (AKI) was assessed by Kidney Disease: Improving Global Outcomes (KDIGO) score on DOE, day 3 and day 7 of colistin therapy.

Results: Survival rate and KDIGO score were assessed in 41 patients and SOFA score was determined in 39 patients. 19.5% of patients had average colistin steady state concentration ($C_{ss, avg}$) between 2.0 – 2.5 mg/L and 68.3% of patients had $C_{ss, avg}$ in the range of 2.6 – 14.5 mg/L. Incidence of AKI while on treatment with colistin was 31.7% (n = 13/41). 11 patients who developed nephrotoxicity had $C_{ss, avg}$ >2.5 mg/L or AUC $_{0\text{-}24h}$ >60 mg.h/L. In patients who had $C_{ss, avg}$ of >2.5mg/L, 40.7% of patients developed AKI (Fisher's exact test, p = 0.16).

85.7% patients survived in low $C_{ss, avg}$ group compared to 57.1% in high $C_{ss, avg}$ group (Fisher's exact test, p = 0.09). Mean (SD) KDIGO score of critically ill patients who survived and not survived were 0.4 (0.8) and 0.8 (1.1) respectively (t-test, p value = 0.1) which implies a trend towards poor clinical outcome with AKI. Only 25.6% of patients had an improvement in SOFA score and colistin $AUC_{0\text{-}24h}$, $C_{ss, avg}$ and trough did not correlate with average SOFA score (R^2 = 0.009, 0.01, 0.0007 respectively).

Conclusion: Survival was higher in patients with low exposure to colistin. It may be useful to monitor colistin concentrations in critically ill patients as colistin concentrations, AKI and clinical outcome seems to be inter-related. Clinical trials with a sample size of at least 30 each in high (>2.5 mg/L) and low $C_{ss, avg}$ needs to be performed to confirm the relationship between $C_{ss,avg}$ and survival.

Keywords: Colistin, critically ill patients, TDM, Nephrotoxicity