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Abstract (poster session)

Model-based optimisation of daptomycin dosing during high-intensity renal replacement therapy

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Objectives: Daily intermittent hemodialysis (IHD) is a renal replacement therapy (RRT) option that may be used to treat patients when the target dose of RRT cannot be provided with the conventional every- other-day schedule. The objective of this study was to establish the optimal dosing regimen of Daptomycin (DAP) for the treatment of serious gram positive infections during daily IHD. Methods: Population pharmacokinetic (popPK) models of DAP in IHD patients and patients with bacteremia were used in this analysis. Daily doses of 3 and 4 mg/kg given 1 hour prior, 1 hour into, and 1 hour before the end of dialysis were evaluated with Monte Carlo Simulation (MCS, n=10000) to assess for the magnitude of drug exposure with daily 2, 3, 4, and 5 hour IHD sessions. To select the optimal regimen based on the duration of dialysis provided, the simulated mean + SD trough levels at 72 hours and AUC48h-72h in dialysis were compared with the simulated mean + SD trough levels at 72 hours and AUC48h-72h for the dose of 6 mg/kg every 24 hours using the popPK model developed in the bacteremia trial. Results: Manufacturer recommended 6 mg/kg DAP regimens should result in mean + SD trough levels and AUC48h-72h values of 9.5 + 8.1 µg/ml, and 441.1 + 275 mg.h/L, respectively. Comparing these means with those expected to be achieved by the suggested daily dialysis regimens, percentage differences of 38% to 64%, and – 5% to 14% in magnitude were noted, for trough levels and AUC48h-72h values, respectively. Summary of optimized dosing recommendations are presented in Table 1. Conclusion: We conclude that the DAP dosing strategies presented here would provide adequate coverage from the efficacy standpoint in daily IHD, as compared to the exposure achieved by the patients of bacteremia trial. Our analysis also showed a definite increase in the magnitude of the expected trough levels using these methods of dosing DAP, which may lead to an increase in the probability of drug related adverse events. Clinicians should carefully weigh risks and benefits of all treatment related effects when managing their patients with the above suggested dosing regimens.

Timing of drug administration	Length of daily dialysis session (hours)			
	2	3	4	5
1 hour prior to dialysis	3 mg/kg	3 mg/kg	4 mg/kg	4 mg/kg
1 hour into dialysis	3 mg/kg	3 mg/kg	4 mg/kg	4 mg/kg
1 hour before the end of dialysis	3 mg/kg	3 mg/kg	3 mg/kg	3 mg/kg