Oral

[O25-7] O25-7: Infectious diseases

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[O25-7-1] Optimal vancomycin dosage in patients with heart failure based on population pharmacokinetics and Monte Carlo simulation

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Background

Heart failure (HF) alters the pharmacokinetics (PK) of various drugs including antibacterial agents such as vancomycin due to decreased cardiac output. There is a lack of information on vancomycin PK in HF patients. For the reason, controlling vancomycin concentration in HF patients has been challenging. The aim of this study was to characterize the PK of vancomycin and propose an optimal vancomycin dosing strategy in HF patients to achieve desirable safety and efficacy targets.

Methods

Left ventricular ejection fraction (LVEF) was used to quantify the level of cardiac function. A total of 399 measurements from 160 patients on vancomycin who also had LVEF assessed during the treatment were identified for this analysis. Supplemental serial PK samples were obtained from 28 patients enrolled in a prospective PK study in addition to routine trough and peak concentration monitoring. Population PK analysis was performed with NONMEM to evaluate potential covariates including demographic information and laboratory parameters. For target attainment analysis, a steady-state trough concentration of 20 mg/L and an AUC/MIC 400 were set as preferred pharmacokinetics and pharmacodynamics targets.

Results

A two-compartmental model best described vancomycin disposition. Covariate analysis in population PK modeling identified estimated creatinine clearance (eCLcr), LVEF and body weight as factors significantly influencing vancomycin clearance. Monte Carlo simulation revealed that, in order to achieve high probabilities of desired targets, an initial dose of 20 mg/kg every 12 h is required for patients with normal renal and cardiac function while 10 mg/kg every 12 h is proposed for HF patients with LVEF of 20% and eCLcr of 30 mL/min. These simulations were in good agreement with clinical observations. Thus, the initial dose need to be reduced for HF patients according to decreased renal and cardiac functions.

Conclusions

Vancomycin clearance decreased in HF patients as cardiac output decreased as well as eCLcr decreased, suggesting that vancomycin clearance is better predicted when both eCLcr and cardiac function are taken into consideration in HF patients. The proposed optimal vancomycin dosing strategy may facilitate a safer and more effective treatment for HF patients. Future prospective studies should be warranted to assess the clinical benefits.