Prolonged used of daptomycin may be necessary in patients with bone and joint infection (BJI). However, little is known about daptomycin pharmacokinetic (PK) variability during prolonged therapy.

The objectives of this study were to describe and quantify inter- and intra-individual PK variability of daptomycin in a cohort of patients with BJI.

This was a retrospective analysis of daptomycin therapeutic drug monitoring (TDM) data obtained from 23 patients receiving daptomycin for BJI. A total of 203 daptomycin plasma concentrations, usually obtained at predose, 0.5-1 h, and 5-6 h post dose, formed 69 individual PK profiles.

The SAEM algorithm implemented in the Monolix software (version 4.4.2, Lixoft, Paris, France) was used to calculate population and individual PK parameters of daptomycin and for covariate analysis by use of population approach and Bayesian estimation. Intra-individual change in daptomycin PK parameters and covariates over therapy were quantified and compared.

Characteristics of the study population are shown in Table 1. A two-compartment, linear PK model best fitted the data. Population and individual predictions correlated very well with observed daptomycin concentrations, as shown in Figure 1.

Estimates of population PK parameters of daptomycin are shown in Table 2. Renal function significantly influenced daptomycin CL. Sex significantly influenced both daptomycin CL and V1, which were 46% and 31% greater in males than in females, respectively. Substantial intra-individual variability in CL and V1 was observed over the TDM period with median CVs of 15% (range, 3-36%) and 11% (3-28%), respectively.

Intravariability changes in daptomycin CL ranged from -58% to +159% and were uncorrelated with corresponding changes in renal function as shown in Figure 2.

Population PK parameter values and influencing covariates identified in this study were consistent with previous reports [1]. However, this study showed significant intra-individual PK variability of daptomycin, which was not predictable from covariates. Daptomycin TDM appears necessary to control individual exposure during prolonged daptomycin therapy.


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