Poster

[P27-1] P27-1: Anti-infective drugs (6): Anti-MRSA and antifungals

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[P27-1-4] Estimation of the duration to reach peak arbekacin concentration by Monte Carlo simulation

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Keywords: arbekacin, peak concentration, Monte Carlo simulation

Background

To date, the efficacy and safety of the aminoglycoside antibiotic arbekacin (ABK) has been evaluated by its serum trough and peak (C_{peak}) concentrations. C_{peak} was originally defined as the peak value of drug concentration in the peripheral compartment. Japanese TDM guidelines recommend that C_{peak} of ABK should be measured when 30 min have passed after the completion of a 30-min intravenous injection. However, it is unknown whether this setting is appropriate for measuring C_{peak} of ABK. In the present study, we validated the duration to reach C_{peak} of ABK by Monte Carlo simulation.

Methods

We hypothesized that changes in serum ABK concentrations obey the 2-compartment model. The pharmacokinetic parameters of ABK were estimated using already-reported ABK concentration data (n = 8) by the least-squares method, which hypothesizes log-normal distribution. Then, the duration to reach C_{peak} after the completion of a 30-min injection for 8 individuals was calculated using the estimated parameters. In addition, the duration to reach C_{peak} for 100,000 artificially generated individuals was calculated by Monte Carlo simulation, which hypothesizes log-normal distribution.

Results

The mean values of duration to reach C_{peak} after the completion of the 30-min injection for 8 individuals and 100,000 artificially generated individuals were calculated as 56.4 min (CV: 100.6%) and 53.7 min (CV: 70.8%), respectively.

Conclusions

In the present study, the mean value of duration to reach C_{peak} after the 30-min injection was estimated to be approximately 60 min, suggesting that the actual duration to reach C_{peak} of ABK is 2-times longer than the duration recommended in Japanese TDM guidelines. In addition, a large CV in the duration to reach C_{peak} was observed, reflecting large inter-individual differences in ABK pharmacokinetics. Indeed, large dispersions were found among the individual parameters calculated using actual ABK concentration data. Taken together, the present study suggested that ABK concentration measured when 30 min have passed after the completion of a 30-min injection is difficult to be considered as C_{peak}, and that individual ABK parameter estimation is needed to estimate the actual duration to reach C_{peak}. Measuring and evaluating the actual C_{peak} may enable more effective ABK therapy.