Poster

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

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[P27-1-8] False prolongation of prothrombin time in the presence of high blood concentration of daptomycin

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Background

Prothrombin time (PT) monitoring is essential during warfarin therapy to minimize bleeding complications and thrombotic events. However, PT can be falsely prolonged by the antimicrobial drug, daptomycin (DAP). False prolongation of PT may lead to the inappropriate reduction of warfarin dose. Although high doses of DAP (>6 mg/kg/day) are recommended for severe infection, they result in high blood concentrations of DAP (>100 mg/L). The extent to which high blood concentrations of DAP interfere with PT remains undetermined. In this study, we examined the effects of high doses of DAP on PT.

Methods

DAP (0–500 mg/L) was added to normal plasma, and plasma with already prolonged PT (abnormal plasma). The PT of plasma samples was measured using a HemosIL RecombiPlasTin 2G instrument. Furthermore, we used a Monte Carlo simulation to calculate the probability of achieving DAP concentrations >100 mg/L, >200 mg/L, and >500 mg/L at 0–48 h after administration of 6–12 mg/kg DAP.

Results

PT increased with increasing DAP concentration. In abnormal plasma, PT international normalized ratio was falsely prolonged from 2.23 to 2.60, from 2.23 to 3.21, and from 2.23 to 6.16 by DAP concentrations of 100 mg/L, 200 mg/L, and 500 mg/L, respectively. The maximum probability of achieving DAP concentrations >100 and 200 mg/L was directly proportional to DAP dose (6 mg/kg DAP, 7.9% for >100 mg/L, 0.6% for >200 mg/L; 8 mg/kg DAP, 24.1% for 100 mg/L, 1.8% for 200 mg/L; 10 mg/kg DAP, 49.8% for 100 mg/L, 4.5% for 200 mg/L; 12 mg/kg DAP, 72.3% for 100 mg/L, 7.8% for 200 mg/L), although the maximum probability of achieving a DAP concentration >500 mg/L was only 0.5%. In contrast, at the trough concentration, the probability of achieving a DAP concentration >100 mg/L was <5.0% in all subjects.

Conclusions

PT should be monitored carefully in patients administered high doses of DAP during warfarin therapy. Ideally, PT should be measured at the trough blood concentration of DAP.