The compatibility of vancomycin with existing and novel β-lactam/β-lactamase inhibitors at clinically relevant concentrations in 5% dextrose in water has not been fully explored to date” Meyer et al (2017).

Abstract:

Objectives: The compatibility of vancomycin with existing and novel β-lactam/β-lactamase inhibitors at clinically relevant concentrations in 5% dextrose in water has not been fully explored to date.

Methods: Vancomycin concentrations tested ranged from 5 to 20 mg/mL. Ceftazidime-avibactam was tested at 8, 20, and 40 mg/mL, ceftolozane-tazobactam at 15 mg/mL, and piperacillin-tazobactam at 28 mg/mL. Compatibility of drug admixtures were tested via both simulated and actual y-site infusion. For the simulated y-site compatibility assessment, 1:1 mixtures of each respective drug were analyzed over 24 hours. Actual y-site infusion followed a 4-hour extended-infusion protocol, with aliquots tested hourly for 4 hours. At all time points, the compatibility of each admixture was determined using 6 different methods: visual, microscopic, Tyndall beam, nephelometric, pH, and microbiologic bioassay assessment. If any admixture failed any one of these 6 assays, it was considered incompatible. Any combination deemed incompatible was filtered through a 0.22 μm filter and reanalyzed to assess impact of particle size.

Results: There were no differences in compatibility categorizations between simulated and actual y-site infusion. There were no changes in compatibility over the time course of any experiment. Ceftazidime-avibactam at 8 mg/mL was incompatible with vancomycin at 5 mg/mL. The maximum compatible vancomycin concentrations were 5 mg/mL and 10 mg/mL with 20 and 40 mg/mL of ceftazidime-avibactam, respectively. Ceftolozane-tazobactam 15 mg/mL was compatible with vancomycin concentrations up to 10 mg/mL. The maximum compatible vancomycin concentration with piperacillin-tazobactam 28 mg/mL was 5 mg/mL. None of the β-lactam/β-lactamase inhibitors tested were compatible with 15 or 20 mg/mL of
vancomycin. None of the admixtures considered incompatible by other methods displayed any decrease in antimicrobial activity as assessed by bioassay. After filtration, all admixtures originally deemed incompatible maintained their visual turbidity and microscopic particulate matter.

Conclusions: Ceftazidime-avibactam prepared at the lowest concentration recommended in the package insert is incompatible with vancomycin. Ceftolozane-tazobactam did not display incompatibility until vancomycin concentrations above 10 mg/mL were tested. Piperacillin-tazobactam at a typical extended-infusion concentration is compatible with vancomycin in D5W. To our knowledge, this is the first study to assess compatibility of antibiotic admixtures via direct measurement of antimicrobial activity. The lack of any decrement in antibacterial activity of any apparently incompatible admixture and maintenance of incompatibility after passage through a 0.22 μm filter may suggest a lack of clinically relevant adverse effects when co-administered. Future compatibility studies should incorporate appropriate methods to accurately assess both efficacy and safety of co-administered drug products.

Reference:


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