

Bactericidal Effects of Fosfomycin Against Daptomycin Resistant Strains of *Staphylococcus aureus*

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Background: Fosfomycin (FOM) and daptomycin (DAP) are two bactericidal antimicrobial agents, which inhibit different steps in the peptidoglycan synthesis and are frequently used in the therapy of serious *Staph. aureus* infections. However, recent literature references evidence of increasing rates of *Staph. aureus* resistance against DAP in the US and elsewhere. This development has been linked to the extensive or prolonged administration of vancomycin or other glycopeptide antibiotics to patients with deep-seated infections, to the critically ill or prosthetic implant recipients. **Methods:** In the present in vitro time-kill experiments, we used three clinical pairs of DAP-susceptible/resistant, methicillin-resistant *Staph. aureus* strains (A6298/A6300, A8819/A8819b, A6224/A6226) and investigated FOM's antimicrobial activity against these pairs of bacteria. Minimum inhibitory concentrations (MICs) were determined before and after completion of the experiments. FOM was used as mono-therapy and in combination with DAP at therapeutic concentrations varying between 10 - 100 µg/ml for FOS, and 1 - 10 µg/mL for unbound DAP. Broth media was supplemented with either 50 mg/L of calcium or 25 mg/L of glucose-6-phosphate. **Results:** After an incubation period of 24 hrs FOM was able to reduce bacterial count of DAP-susceptible and DAP-resistant *Staph aureus* pairs by more than 3-log compared to the starting inoculum of approximately 5×10^7 CFU/mL. DAP's MICs of *Staph. aureus* pairs were ≤ 0.5 µg/mL for the progenitor strain and ≥ 4 µg/mL for the DAP-resistant isolate. FOM was highly active against DAP-resistant *Staph. aureus* strains. In the present setting, the combination of DAP plus FOM did not further improve overall antimicrobial activity, suggesting that a synergistic or additive effect may not be detected for DAP-resistant *Staph. aureus* strains, if FOM and DAP are used in combination. **Conclusion:** At therapeutic concentrations, FOM killed DAP-resistant *Staph. aureus* strains highly effectively. FOM could therefore be considered a therapeutic option in treating these types of infections.