Synergistic Comparison of Ceftobiprole and Ceftaroline with Daptomycin for Biofilm Prevention

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Background
Ceftobiprole is a fifth-generation cephalosporin demonstrating increased activity against a broad spectrum of bacteria, including Methicillin-resistant S. aureus (MRSA). MRSA is a major concern following orthopedic surgeries, notorious for developing treatment resistant biofilms. Ceftaroline is currently used with daptomycin to limit biofilm formation but has a limited spectrum of activity. Ceftobiprole has demonstrated synergy with daptomycin; however its synergy in comparison to ceftaroline and its efficacy against biofilms has yet to be characterized.

Objectives
This study aims to assess ceftobiprole's synergy with daptomycin in comparison to ceftaroline. Further, this study aims to assess ceftobiprole's efficacy at preventing biofilm formation in combination with daptomycin.

Methods
Checkerboard assays were performed to compare synergy of daptomycin with ceftobiprole and ceftaroline. Both were administered with daptomycin to catheters treated with Methicillin-resistant USA300 strain LAC to assess efficacy against *in vitro* biofilm formation and compared to efficacy of single antibiotic administration.

Results
Ceftaroline demonstrated clearer synergy with daptomycin than ceftobiprole, however additional trials are needed to clarify this relationship. Both combinations were more effective than single drug administration against biofilm formation. By D3, ceftaroline and ceftobiprole with daptomycin were not significantly different from each other in terms of elimination of biofilms.

Conclusions
Ceftobiprole may be a viable alternative to ceftaroline with daptomycin due to its similar activity against MRSA biofilm formation. As the majority of implant-related infections in an orthopedic setting involve biofilm formation, additional options with broader spectrum coverage could improve patient outcomes. However, ceftobiprole's activity must be further assessed *in vivo* to fully assess its potential benefits.

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