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Distribution and antimicrobial activity of fosfomycin in the interstitial fluid of human soft tissues.

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Source

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Abstract

Fosfomycin is a broad-spectrum antibiotic which is established as therapy for uncomplicated lower urinary tract infections. In addition, preliminary data indicate that fosfomycin has a potential role in the treatment of soft tissue infections. However, the use of fosfomycin has not been established for this condition, and it is unclear whether the level of fosfomycin penetration into human soft tissues is high enough to eradicate relevant pathogens. To better characterize the antibiotic potential of fosfomycin, we applied a combined in vivo pharmacokinetic-in vitro pharmacodynamic model to human volunteers. For this purpose fosfomycin concentrations in vivo in the fluid of the interstitial space of human soft tissues were measured by microdialysis following intravenous infusion of 4 or 8 g of fosfomycin (n = 6). Subsequently, bacterial isolates with relevance for soft tissue infections were exposed to concentrations according to the in vivo pharmacokinetic profile in the interstitial space fluid obtained by microdialysis. Our experiments indicated a high degree of soft tissue penetration for fosfomycin, with ratios of the area under the concentration-time curve from 0 to 8 h for muscle (AUC(0-8(muscle)))/AUC(0-8(serum)) of 0.48+/-0.08 and 0.53+/-0.04 and ratios of AUC(0-8(adipose tissue))/AUC(0-8(serum)) of 0.74+/-0.12 and 0.71+/-0.11 following administration of 4 and 8 g, respectively. In corresponding in vitro simulation experiments with selected isolates of Staphylococcus aureus, Enterobacter cloacae, and Serratia marcescens for which MICs were 16 microg/ml, organisms were undetectable after a single dosing interval. Fosfomycin exhibits a strong ability to penetrate into the fluid of the interstitial space of soft tissues and reaches levels sufficient to substantially inhibit the growth of relevant bacteria at the target site. We therefore conclude that fosfomycin might qualify as an alternative candidate for the therapy of soft tissue infections.

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