

Efficacy and safety of high-dose daptomycin (>6mg/kg) for complicated bone and joint infections and implant-associated infections caused by Gram-positive bacteria

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Abstract

Objectives: Daptomycin at high dose may improve treatment outcome. We evaluated the efficacy and safety of high-dose daptomycin treatment (>6 mg/kg) in complicated infections with Gram-positive bacteria.

Methods: We included patients older than 18 years diagnosed with complicated staphylococcal and enterococcal infections involving implants, bone or joints, soft tissue or bloodstream. Complicated infections were defined as insufficient response to previous antibiotic, reduced susceptibility of the pathogen to glycopeptides, renal insufficiency, presence of implant or allergy to glycopeptides. Daptomycin was administered intravenously at >6 mg/kg every 24 h (or every 48 h, if creatinine clearance was <30 mL/min). Patients were evaluated for efficacy during hospital stay and after discharge. Cure was defined as absence of clinical signs and symptoms of infection after discontinuation of the antimicrobial treatment.

Results: In total, 72 patients (median age, 67 years; 67% male), hospitalised at Lausanne University Hospital (Lausanne, Switzerland) between January 2009 and May 2012 with diagnosis of implant-associated infections (n = 37; 51%), bone and joint infections (n = 26; 36%), complicated soft tissue infections (n = 5; 7%) and bloodstream infections (n = 4; 6%) were included. *Staphylococcus aureus* was isolated in 38 (46%), coagulase-negative staphylococci in 36 (43%) and enterococci in 9 (11%) patients. The median daily dose was 9.6 mg/kg (range 6.1–14.9 mg/kg), the median cumulative dose was 11.3 g (range 2.7–59.3 g) and the median duration of daptomycin therapy was 17 days (range 5–89 days). Patients were followed-up for a median of 21 months (range 10 days to 3.5 years). One-year infection-free survival was 87% (95% confidence interval 77–93%) and no additional failures occurred in the following 2 years. Thirteen patients (18%) had an adverse event possibly related to daptomycin: asymptomatic creatine phosphokinase increase (CPK) (n = 6), eosinophilic pneumonia (n = 3), generalized rash (n = 2), rhabdomyolysis (n = 1) and acute renal failure (n = 1). All adverse events reversed completely.

Conclusion: The efficacy of high dose daptomycin in complicated gram-positive infections was high and symptomatic adverse events occurred in 10% of the patients.

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