

"Daptomycin defined daily dose correlates with increasing MICs in *Enterococcus faecium* isolates from bloodstream infection – a 6-year survey"

A. Egli¹, E. Kuenzli¹, H. Schmid¹, A. Widmer¹, D. Goldenberger¹, R. Frei¹, M. Weisser¹

¹Division of Clinical Microbiology- University Hospital Basel, Basel, Switzerland

Introduction: *Enterococcus faecium* has become a major cause of nosocomial bloodstream infection (BSI). Treatment options are limited, for vancomycin-resistant and susceptible enterococci (VRE/VSE). Daptomycin is one of the few remaining treatment options, but emergence of resistance may occur with increasing use of daptomycin. Therefore, we compared the mean MICs of isolates with the use of daptomycin to evaluate changes of susceptibility over time.

Methods: We prospectively collected all isolates of *E. faecium* from positive blood cultures with 2008-2014. The minimal inhibitory concentrations (MICs) of daptomycin for all *E. faecium* isolates were determined using Etests (bioMérieux, range 0.016-256 mg/L). The in-hospital annual use of daptomycin was determined using defined daily dose (DDD) of daptomycin per 100 patient days were calculated for the same time period and correlated with the mean MIC values.

Results: In total, 202 *E. faecium* isolates from 161 patients were analysed. The mean MIC for daptomycin was 2.51 mg/L (SD 1.28 mg/L). 24/202 (12%) isolates had a MIC of 4 mg/L. 6/202 (3%) isolates had >4 mg/L and showed resistance according to CLSI breakpoint.

The usage of daptomycin increased from 0.04 (2007) to 1.26 DDD per 100 patient days (2013), which corresponds to a 31.5-fold increase. The DDDs and MICs of daptomycin showed a positive correlation over time ($R^2=0.32$, $p=0.07$, **Figure 1A**).

In 31/161 (19%) patients, a recurrent or ongoing bacteremia with in median one follow-up sample (range 1-3) was found. The median duration between first and following positive blood culture was 23.5 days. In 17/31 (55%) cases, the MIC for daptomycin increased ($p=0.0019$, **Figure 1B**, mean 2.1 to 3.2 mg/L). 5/17 (29%) isolates became resistant.

Conclusions: In BSI, 3% of *E. faecium* isolates showed resistance against daptomycin, an additional 12% showed MICs at the clinical breakpoint for resistance. Emergence of resistance was related to the use of daptomycin on an individual as well as the overall use of daptomycin.

Figure 1. A Daptomycin MICs in samples with continuing bacteremia. **B.** Development of DDDs and MICs of daptomycin over time.

