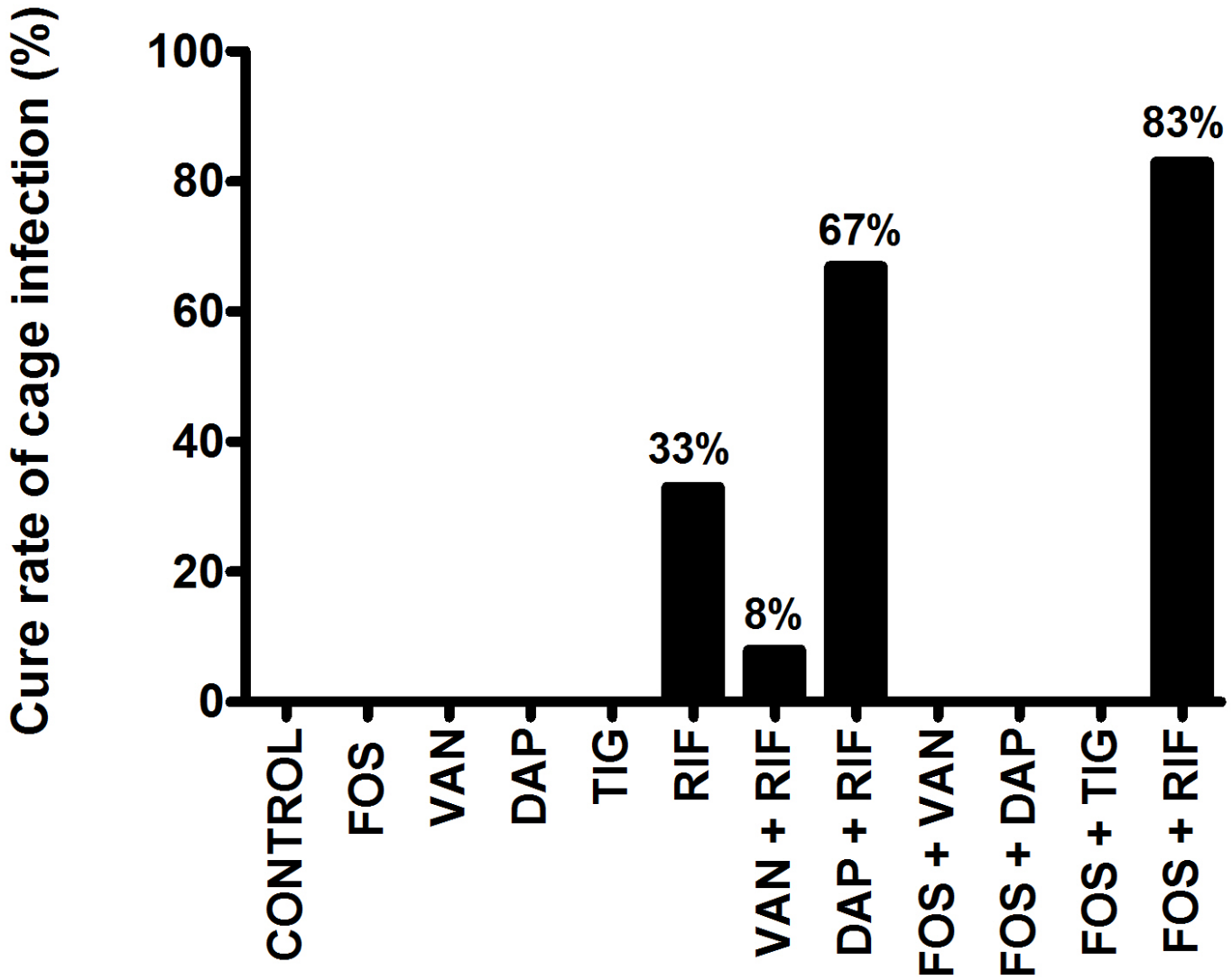
P2062

Abstract (poster session)

High efficacy of fosfomycin-rifampin combination against methicillin-resistant Staphylococcus aureus in an experimental model of foreign-body infection

R. Mihailescu*, U. Furustrand Tafin, B. Bétrisey, L. Rio, E. Maiolo, O. Borens, A. Trampuz (Bucharest, RO; Lausanne, CH)

Objective: Increasing antimicrobial resistance limits available options for treatment of methicillin-resistant Staphylococcus aureus (MRSA), especially when associated with implants. We evaluated the efficacy of fosfomycin (FOS), vancomycin (VAN), daptomycin (DAP), tigecycline (TIG) and rifampin (RIF), alone and in combinations, against MRSA in a foreign-body infection model. Methods: Teflon cages (32 x 10 mm) were subcutaneously implanted in guinea pigs (weight 450-500 g). Cages were infected by percutaneous injection of 3 x 10^6 CFU MRSA (ATCC 43300). 72 h after infection, treatment was administered for 4 days by intraperitoneal injection of FOS 150 mg/kg, VAN 15 mg/kg, DAP 50 mg/kg (corresponding to 10 mg/kg in humans), TIG 10 mg/kg, RIF 12.5 mg/kg or their combinations (12 cages per treatment regimen). Antibiotics were administered every 12 h, except DAP that was given every 24 h. 5 days after end of therapy, bacteria were counted in aspirated cage fluid and compared to the concentration before treatment to evaluate the antimicrobial effect on planktonic MRSA.Cages were then aseptically explanted and cultured in TSB for 48 h to determine the eradication of MRSA, expressed as cure rate (percentage of cages without growth of MRSA). Results: The MIC was 1 µg/ml for FOS, 1 µg/ml for VAN, 0.125 µg/ml for DAP, 0.125 µg/ml for TIG and 0.04 µg/ml for RIF. Bacterial counts of 6.6 x 10^6 measured on day 3 after infection were reduced by (median log CFU/ml) 0.3 log with FOS alone, 2.2 log with FOS+VAN, 3.8 log with FOS+DAP, 2.2 log with FOS+TIG, >6.0 log with DAP+RIF and >6.0 with FOS+RIF. Figure shows the cure rate of individual treatment regimens. In untreated animals (controls), no spontaneous cure occurred. Among single-therapy regimens, only RIF showed cure in 4/12 cages (33%). Among combination regimens, only RIF-containing regimens demonstrated cure in 1/12 cages (8%) with VAN+RIF, in 8/12 cages (67%) with DAP+RIF and in 10/12 cages (83%) with FOS+RIF. No emergence of resistance to FOS was observed in failures receiving single or combination treatment regimens (MIC <=16 µg/ml). Conclusion: The highest cure rate of MRSA cage-associated infection was achieved with the combination FOS+RIF (83%), which was superior to other RIF-containing combinations. No emergence of FOS resistance was observed. These data suggest that addition of FOS to RIF might further improve the treatment outcome of MRSA implant-associated infections.


Cure rate of cage infection (%)
100
80
60
40
20
0
33%
8%
67%
83%
CONTROL
FOS
VAN
DAP
TIG
RIF
VAN + RIF
DAP + RIF
FOS + VAN
FOS + DAP
FOS + TIG
FOS + RIF