

Efficacy of Daptomycin Against *Staphylococcus epidermidis* in an In Vitro-Infected Fibrin Clot Model: Comparison with Vancomycin

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Background: Vancomycin (VAN) is considered as the standard regimen for the treatment of staphylococcal infection. Nevertheless, slow response rates and failures have been reported. The objective of this study was to evaluate and compare the efficacy of daptomycin (DAP) and VAN against methicillin-resistant *S. epidermidis* strains (MRSE), not in planktonic state, but in a complex environment using a fibrin clot model.

Methods: Three MRSE were tested (two of them were ica+ and produced biofilm and one was ica- and did not produce biofilm). Infected fibrin clots were prepared by mixing 400 μ L of human plasma, 125 μ L of human thrombin and 50 μ L of MRSE at 10^6 CFU/mL in a sterile siliconized tube containing a sterile monofilament line. Five fibrin-clots per strain were performed and three experiments (in triplicates) were performed. After 24h-incubation at 37°C, the fibrin clots were washed and placed in a new tube containing either DAP at 25mg/L or 100mg/L either VAN at 25mg/L or 200 mg/L or no antibiotic. After 0h (control) and 24h of incubation, the fibrin clots were weighed, homogenized and plated on MH plates. Surviving bacteria (SB) were counted and expressed as \log_{10} CFU per gram of fibrin clot.

Results: Results were as follows:

	Mean \pm SD \log_{10} CFU/g of fibrin clot				
Strains	Control	DAP25mg/L	DAP100mg/L	VAN5mg/L	VAN200mg/L
MRSE1 ica+biofilm+	10.0 \pm 0.4	2.2 \pm 0.1 ^{a,c}	<2.0 \pm 0.1 ^{a,c}	9.0 \pm 0.6	8.5 \pm 0.3
MRSE2 ica+biofilm+	9.0 \pm 0.4	4.5 \pm 0.2 ^{a,c}	2.3 \pm 0.1 ^{a,c}	6.3 \pm 0.5 ^b	6.1 \pm 0.3 ^b
MRSE3 ica- biofilm-	10.0 \pm 0.3	2.2 \pm 0.1 ^{a,c}	<2.0 \pm 0.1 ^{a,c}	7.9 \pm 0.3 ^b	7.1 \pm 0.3 ^b

^a: $P < 0.001$ vs controls. ^b: $P < 0.05$ vs controls. ^c: $P < 0.05$ vs VAN5mg/L and VAN200mg/L.

Conclusion: 1. After 24h-incubation, SB were significantly lower in all fibrin clots treated by daptomycin whatever the concentration is. 2. Daptomycin has exhibited a better activity in fibrin clot against MRSE than vancomycin. Daptomycin could be the antibiotic of choice for treating severe infections.