The Clinical Difference between Minimum Inhibitory Concentration and Minimum Biofilm Eradication Concentration

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INTRODUCTION: Dosing of antimicrobials in the treatment of prosthetic joint infection (PJIs) is guided by the Minimum Inhibitory Concentration (MIC) of identified pathogens, determined by testing planktonic, free-floating bacteria. However, most PJIs are caused by bacteria within biofilm, which are microcolonies of bacteria encapsulated in a protective matrix that adhere to the surface of the prosthesis and surrounding tissue. Biofilms can have up to a 50,000-fold increase in the antimicrobial tolerance when calculated using the Minimum Biofilm Eradication Concentration (MBEC). We quantified the MBEC of methicillin sensitive *Staphylococcus aureus* (*S. aureus*) biofilms from clinical isolates obtained during Debridement, Antibiotics, and Implant Retention (DAIR) and compared them to the calculated MIC.

METHODS:

With IRB approval, clinical isolates of methicillin sensitive *S. aureus* from DAIR revision arthroplasty cases collected over two years were identified from the clinical microbiology registry of our tertiary medical center. The MIC of each isolate was determined using the Vitek 2 Susceptibility Panel. To quantify the MBEC, four clinically relevant antimicrobials were tested: Daptomycin (Dpt), Doxycycline (Dox), Oxacillin (Ox), and Vancomycin (V). Inoculums of each isolate were standardized and introduced into a 96-well MBEC Assay device, in which pegs remain immersed in the inoculum to form a biofilm. Pegs were then submerged in the antibiotics challenge plate for 20-hours. The remaining biofilm was determined via sonication and the colony forming units (CFU) were quantified in triplicate. Concentrations at which no viable bacteria remained were identified as the MBEC.

RESULTS:

The MBEC of 5 clinical isolates was determined using this method. The MIC values for Dpt (0.25 µg/mL), Dox (<0.5 µg/mL), and V (1 µg/mL) were the same for all isolates. The MIC values for Ox ranged from ≤0.25 to 1 µg/mL. The MBEC is presented as a range, including the last antibiotic concentration that had bacterial growth and the first concentration where no bacterial growth was detected, to account for possible MBEC values between the two. For the isolates tested, the highest MBEC ranges were: >27,500 µg/mL for Dpt, 10-100 µg/mL for Dox, >27,000 µg/mL for Ox, and 4,500-5,000 µg/mL for V.

DISCUSSION AND CONCLUSION:

For each isolate tested, the clinical MIC was lower than the quantified MBEC. This finding highlights the limited value of the MIC when guiding clinical decision making. When selecting an optimal antibiotic treatment, both MIC and MBEC values should be considered. Further evaluation of the clinical impact of these disparate values needs to be assessed. Methods to quantify the MBEC in a clinical setting need to be developed.

	MSSA Clinical Isolate		Values reported in the Literature	
	Ox (µg/mL)	V (µg/mL)	Ox (µg/mL)	V (µg/mL)
MIC	0.5	1	0.5	1
MBEC	>27,000	4,500-4,000	25,600	644-3,200

Table 1. MIC and MBEC values for Oxacillin and Vancomycin for a tested clinical isolate (left) and *S. aureus* isolates described in literature (right). These values are reported in µg/mL.