Evaluating the Minimum Biofilm Eradication Concentration (MBEC) of Oxacillin for *Staphylococcus aureus* Isolates from Acute, Sub-Acute, and Chronic Prosthetic Joint Infections

Paris Taylor[1], Elizabeth Stewart [1], Beethi Sinha[1], Matthew Dietz[1]
[1]West Virginia University School of Medicine, Morgantown, WV
Pt00009@mix.wvu.edu

DISCLOSURES: Paris E Taylor (N), Elizabeth Stewart (N), Beethi Sinha (N), Matthew J Dietz

INTRODUCTION: Treatment of prosthetic joint infections (PJIs) remains a major challenge in the field of orthopaedic surgery. *Staphylococcus aureus (S. aureus*) is the most common causative pathogen responsible for PJI. Multiple virulence factors contribute to the pathogenicity of *S. aureus*, including antibiotic resistance and the ability to form biofilms. Biofilms are known to provide increased antimicrobial tolerance, quantified by the minimum biofilm eradication concentration (MBEC). The minimum inhibitory concentration (MIC) has been utilized to define the phenotypic resistance to antibiotics. To date, no standardized protocol for measuring the MBEC has been adopted in the clinical setting and the knowledge of how the antimicrobial tolerance of biofilms differ based on the chronicity of the infection is limited. In this study, we aimed to define the MBEC of oxacillin for methicillin-sensitive (MSSA) and methicillin-resistant (MRSA) *S. aureus* isolates from patients with PJIs that varied in chronicity.

METHODS: With IRB approval, clinical isolates of MSSA or MRSA obtained from revision hip, knee, and shoulder arthroplasty cases were identified and collected from the clinical microbiology registry of our tertiary medical center. 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 an antibiotic challenge plate containing increasing concentrations of oxacillin for 20 hours. The remaining biofilm was dislodged via sonication and the colony forming units (CFU) were quantified. Concentrations at which no viable bacteria remained were identified as the MBEC. Patient data was gathered and used to determine the chronicity of the infection at the time each isolate was collected. Infections were categorized as acute (<3 months post-surgery), sub-acute (3-12 months post-surgery), and chronic (>12 months post-surgery). Each infection was classified based on the interval between the TJA or last surgery with a negative culture and the subsequent revision surgery for infection. The Mann-Whitney U test was used to compare the MBEC values between MSSA and MRSA isolates. Additionally, the MBEC values among isolates from acute, sub-acute, and chronic infections within each pathogen group were compared.

RESULTS: The MBEC of 30 isolates from knee, hip, and shoulder PJIs was determined. The recorded MBEC value for oxacillin ranged from 4 µg/mL to 27,000 µg/mL, with several isolates exceeding the upper limit. Within each pathogen group, the MBEC values did not differ significantly among acute, sub-acute, and chronic infections (MSSA: P=0.6903; MRSA: P>0.9999).

DISCUSSION: For majority of the isolates included in this study, the oxacillin MBEC values were greater than 27,000 µg/mL, exceeding concentrations that can be achieved clinically. Despite the presence or absence of methicillin resistance, no significant differences in MBEC values were found between MSSA and MRSA isolates across all levels of chronicity. These results suggest that biofilm-associated antibiotic tolerance is independent of phenotypic resistance and infection stage. Further evaluation of the clinical impact of these values needs to be assessed before methods to quantify the MBEC can standardized and adapted into a clinical setting.

SIGNIFICANCE/CLINICAL RELEVANCE: This study highlights the need for biofilm-specific susceptibility testing to guide treatment strategies for PJIs caused by biofilms.

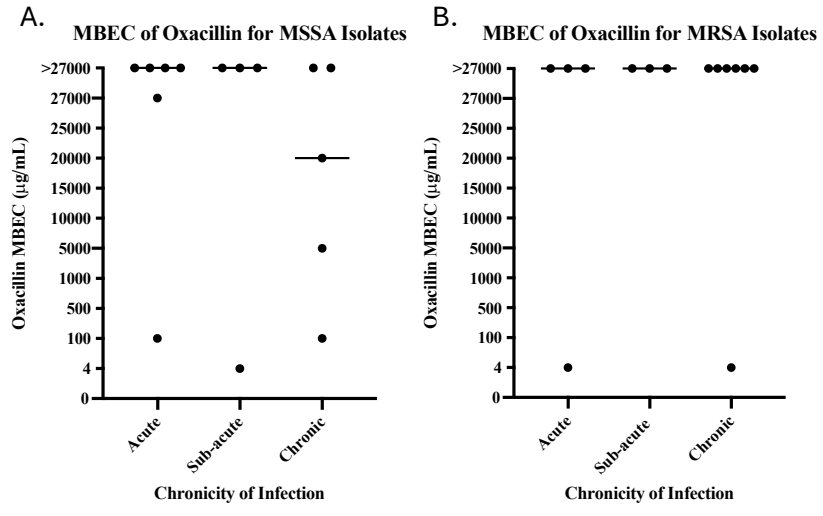

Figure 1: Comparison of MBEC values across all levels of chronicity. The MBEC of oxacillin for (A) MSSA and (B) MRSA isolates from acute, sub-acute, and chronic PJIs were compared using the Kruskal-Wallis test for multiple comparisons.