Voltage Controlled Electrical Stimulation Combined with Povidone-Iodine Treats the Implant Associated MRSA Bacterial Burden

Jacob Opalinski, Bernadette Zumpano, Scott Nodzo, Mary Canty

INTRODUCTION:

Periprosthetic joint infection (PJI) is a devastating outcome of total joint arthroplasty (TJA). Debridement, antibiotic, and implant retention (DAIR) has been used clinically to treat patients; however, DAIR success varies widely (20-90%). Previous research indicates cathodic voltage-controlled electrical stimulation (CVCES) can reduce implant-associated methicillin-resistant *Staphylococcus aureus* (MRSA). CVCES technology has been commercialized and continues to be evaluated in preclinical models. This study evaluated MRSA viability after CVCES and 10% povidone-iodine irrigation on cemented and uncemented commercially available patellofemoral implants.

METHODS: Commercially available size 2 patellofemoral implants were sterilized prior to use. Experiments were conducted with the CA-127 MRSA orthopedic isolate. Fresh cultures were prepared in 5mL of TSB to an OD_{600} of 0.05, incubated overnight, then added to 500mL TSB media containing implants with and without commercially available bone cement. Implants were incubated on a magnetic stir plate at 37°C and 130rpm. After 24hrs, the TSB media was exchanged for fresh media and then incubated an additional 24hrs. CVCES utilizes a three-electrode system consisting of a working (implant), counter (platinum), and reference electrode (Ag/AgCl). Implants treated with CVCES received a -1.9V vs. Ag/AgCl treatment for 24hrs. Custom agar flow chambers were fabricated (3.0% agar in sterile saline (0.9% NaCl)). After incubation, implants were rinsed in sterile PBS to remove loosely adherent cells. Implants that served as controls and wash alone (3min soak 10% povidone-iodine wash) were harvested immediately after growth incubation. Remaining implants were placed into flow chambers supplying fresh TSB at 0.08mL/min, and treated with CVCES alone, or 10% povidone-iodine+CVCES. Implants were washed in sterile PBS+0.1% saponin, sonicated, and dilution plated for colony forming unit (CFU) enumeration. Three independent samples were evaluated in each treatment condition. A one-way ANOVA followed by Tukey post-hoc compared log-transformed CFUs across conditions. If significant Levene's test, a Welch's test followed by a Games-Howell post-hoc test was performed.

RESULTS:

Results are shown in Figure 1. 10% povidone-iodine+CVCES showed a 7-log reduction in MRSA viability, to below detection limits, on uncemented implants. Cemented implants showed 97.6% more growth than on uncemented implants ($1.88x10^9$ vs. $4.50x10^7$ CFU/implant, Figure 1B). As compared to controls, treatment with 10% povidone-iodine alone resulted in a 93.1% reduction in MRSA viability on uncemented implants ($3.10x10^6$ vs. $4.50x10^7$ CFU/implant, $p=0.001$) and a 95.8% reduction on cemented implants ($7.83x10^7$ vs. $1.88x10^9$ CFU/implant, $p=0.002$). CVCES treatment was 99.9% effective at reducing MRSA bioburden from controls (Uncemented: $1.50x10^2$ vs. $4.50x10^7$ CFU/implant, $p<0.001$, Cemented: $6.17x10^4$ vs. $1.88x10^9$ CFU/implant, $p<0.001$). CVCES combined with 10% povidone-iodine reduced MRSA to below detectable levels, a 99.9% increase in efficacy over 10% povidone-iodine irrigation alone on both cemented and uncemented implants.

DISCUSSION AND CONCLUSION:

PJI following orthopaedic surgery is devastating to the patient and early DAIR intervention has widely variable success rates. This study shows CVCES can increase the efficacy of a 10% povidone-iodine irrigation when used on implant associated bacteria by 99.9%, and clear bacterial burden to below detection in the absence of cement. This study highlights the problematic nature of bone cement during infection and its recalcitrance to irrigation techniques. CVCES is a promising technology to improve patient outcomes and may be combined with adjuvant treatments during a DAIR procedure.

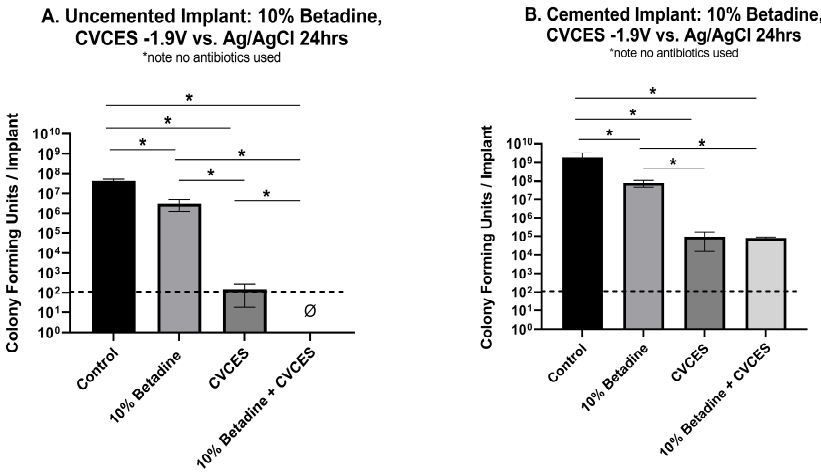

Figure 1: Colony forming units per implant of MRSA enumerated from (A) Uncemented and (B) Cemented Implants for control, exposure to 10% betadine, treatment with CVCES, and combined treatment of 10% betadine followed by CVCES treatment. * indicates p<0.05