Electrical Stimulation Decreases Implant Bacterial Burden in an in vivo Model of Periprosthetic Joint Infection

Scott R. Nodzo, M.D., Menachem Tobias, MS, Lisa Hufnagel, Nicole Luke-Marshall, PhD, Ross Cole, BS, Anthony A. Campagnari, PhD, Mark Ehrensberger, PhD.
University at Buffalo, Buffalo, NY, USA.

Disclosures:

Introduction: Infection rates of primary joint arthroplasty have been reduced to 0.3-2% with modern aseptic techniques, but this rate may reach 20% in some revision procedures. Currently, the gold standard for treating delayed periprosthetic joint infections (PJI) remains a two-staged revision arthroplasty due to bacterial biofilm formation on the retained components. Unfortunately, this treatment method involves multiple surgical procedures and removal of implants that may be well fixed. Due to the limitations of a two-staged revision arthroplasty, alternative methods for treating PJI must be investigated. We previously reported that cathodic voltage-controlled electrical stimulation of titanium induces significant in vitro bactericidal activity versus Gram-negative Acinetobacter baumannii in both a biofilm and planktonic form [1]. In the present study, we evaluated the antimicrobial effects of cathodic voltage-controlled electrical stimulation of a titanium implant in a previously established rodent PJI model [2]. We hypothesized that electrical stimulation of the implant would reduce the bacterial burden on the implant and the surrounding bone tissue when compared to control animals that received no electrical stimulation.

Methods: Prior to the start of the study, approval from our Institutional Animal Care and Use Committee (IACUC) was obtained. Sixteen adult male Long-Evans rats weighing 175-250 grams had a custom made, commercially pure, sterile titanium implant surgically placed into the right shoulder via a ventral peri-axillary approach. The implant was placed through the central aspect of the humeral head and extended approximately 5-7 mm past the lateral aspect of the humeral shaft. At the time of implantation, 1x10^6 colony forming units (CFU) of a clinical strain of a known biofilm forming methicillin resistant Staphylococcal aureus (NRS70) was injected into the joint and implant drill hole just prior to rotator cuff and deep tissue closure. Rats were maintained for 6-7 days postoperatively to develop a localized PJI. After this incubation period, the animals were randomly selected for either the control group (n=8) that received no electrical stimulation or the treatment group (n=8) that received electrical stimulation. In the treatment group, electrical contact was made to the lateral extension of the titanium implant (working electrode) via a skin incision. In addition, a sterile platinum wire (counter electrode), and a sterile Ag/AgCl wire (reference electrode) were placed subcutaneously at separate sites adjacent to the incision used to access the titanium implant. This standard three-electrode configuration was connected to an external potentiostat to apply -1.8V vs Ag/AgCl to the titanium implant for one hour. Following stimulation, the implant was extracted and a section of the humeral head was harvested. The implant and bone were sonicated for five minutes in 0.1% saponin to release adherent bacteria before being serially diluted and plated for enumeration of CFUs/mL. Peripheral blood samples were cultured for bacteria on standard agar plates. In order to determine if the electrical stimulation had a detrimental effect on the surrounding bone, a pathologist blinded to the rat condition, evaluated serial slices of trichrome and hematoxylin and eosin (H&E) stained humeral head and diaphyseal sections. Student t-tests were used to analyze bone and implant associated CFUs between the groups.

Results: The implant associated CFUs enumerated from the treatment group were significantly less than those from the control group (1155 ± 2276 vs. 54750 ± 33949, respectively; p<0.001)(figure 1). In addition, the bone associated CFUs enumerated from the treatment group were significantly less than those from the control group (14755 ± 14777 vs. 114688 ± 156112, respectively; p<0.001)(figure 2). Overall, the electrical stimulation reduced the bone-associated CFUs by approximately 90% and implant-associated CFUs by approximately 99%. Evaluation of the humeral head histologic sections revealed no regions of bone destruction from the electrical stimulation. In both groups, new bone growth around the implant tract was observed. The peripheral blood cultures at the time of harvest were negative in all animals, indicating that the infection was localized to the shoulder/implant.

Discussion: We have shown that one hour of cathodic voltage-controlled electrical stimulation applied to a titanium implant in a PJI rodent model can significantly decrease the CFUs of clinically relevant bacteria on both the titanium implant and the surrounding bone. The mechanism of this antimicrobial effect is not definitively known, but we hypothesize it is related to the faradaic modification of the local electrochemical microenvironment adjacent to the implant. Specifically, at -1.8V vs Ag/AgCl the cathodic half-cell reactions consist of water reduction and to a lesser extent oxygen reduction. Both of these reactions act to increase the local pH and lower oxygen tension. In addition, non-faradaic (surface charging) processes may also contribute to dispersing the bacteria from the implant. While further work is needed to clarify the mechanism of action, these initial, proof-of-principle results are compelling in that a relatively brief application of electrical stimulation to an infected implant was able to
decrease the bacterial burden of the implant and the bone. In addition, it is also encouraging that, according to our histologic evaluation, the electrical stimulation had no immediate adverse effects to the surrounding bone. Future work with this model will focus on further decreasing the bacterial load in the bone and on the implant with the use of perioperative antibiotics in hopes of providing a rationale for retention of components during PJIs.

**Significance:** Cathodic voltage-controlled electrical stimulation may provide an effective and minimally invasive treatment option for PJIs.

**Acknowledgments:** CDMRP/Peer Reviewed Orthopedic Research Program, Idea Development Grant W81XWH-10-1-0696 and Bruce Holm Memorial Catalyst Grant.

**References:**
Figure 1  Implant Bacterial Burden

Stimulation (-1.8V)  Control

CFUs/mL

10^5
10^4
10^3
10^2
10^1
10^0
Figure 2

Bone Bacterial Burden

CFUs/mL

Stimulation (-1.8V)  Control

ORS 2014 Annual Meeting
Poster No: 1947