CORR Insights®: Cathodic Voltage-controlled Electrical Stimulation Plus Prolonged Vancomycin Reduce Bacterial Burden of a Titanium Implant-associated Infection in a Rodent Model

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Where Are We Now?

Periprosthetic infections present a major challenge to patients and treating physicians.

Antibiotic therapy and limited débridement with implant retention fail to eradicate chronic infections and have limited efficacy in acute infections, especially when duration of symptoms exceeds 5 days, infection is caused by methicillin-resistant Staphylococci, or a sinus tract is present [7, 10]. The key pathogenetic mechanism for failure of management in these cases is formation of biofilm on the surface of retained implants. This community of bacterial cells, embedded in a matrix of extracellular polymeric substance and attached to the foreign body surface, is characterized by high resistance to antibiotics and host defense mechanisms [1, 11]. Application of electric current has been shown in vitro to have a direct adverse effect on bacterial biofilms, reducing the number of viable bacteria in a time-dependent and dose-dependent manner [3]. Animal models of implant-associated infections have confirmed the action of electric current against biofilm cells [4, 5]. Application of electric current exhibits a synergistic effect with antibiotic administration in vitro, which has been called the bioelectric effect [2]. A recent study demonstrated in an animal model of implant-associated infection that cathodic electrical stimulation of titanium implants combined with administration of vancomycin for a week was able to reduce the colony-forming units (CFUs) on the implant by 99.8% compared to controls [9].

However, successful management of periprosthetic infection with retention of implants requires eradication of the infecting pathogens, not just a substantial reduction in the number of viable cells. It remains unknown whether eradication of biofilm infections would be possible using this approach and which specific treatment variables would be necessary to achieve that.
The current study by Nodzo et al. evaluated the use of prolonged (5 week) administration of vancomycin combined with either one or two electrical stimulation treatments in rat model of implant-associated infection caused by methicillin-resistant Staphylococcus aureus. The authors demonstrated that the combination of vancomycin with one electrical stimulation treatment resulted in undetectable implant CFU in four of five animals and undetectable bone CFU in all five animals. In addition, no deleterious histological effects of treatment were observed.

Where Do We Need To Go?

These results are promising and I commend the authors for their work. Even so, important questions remain in order to fully evaluate the potential of this treatment against implant-associated infections. As the authors point out, undetectable CFU levels do not necessarily mean that the infection was eradicated, therefore absence of viable biofilm bacteria after conclusion of treatment stills needs to be confirmed. Moreover, treatment was initiated early (6 days) after inoculation of the implant with pathogens. Future studies might evaluate the efficacy of treatment in infections of longer duration with more-mature biofilms.

A pathogen-specific combination of electrical stimulation and antibiotic therapy could maximize the bioelectric effect. The best combination of electrical stimulation variables (such as magnitude and duration) and antibiotic therapy variables (such as agent, dosage, duration, and combinations of agents like adding rifampin for Staphylococcal infections) against different pathogens remains to be determined. The addition of agents, such as dispersin B or quorum-sensing inhibitors, may have a synergistic effect and improve treatment efficacy.

Furthermore, electrical stimulation of implants needs to be further evaluated for potential complications, such as tissue toxicity and adverse effects on the implant, especially after prolonged application. Delivery of electrical current by placing an electrode on the implant through the soft tissue envelope may provide a conduit for contamination of the implant.

How Do We Get There?

These questions will have to be addressed in multiple further animal studies in order to assess in detail the efficacy and safety of electrical stimulation and antibiotic therapy and determine the optimal indications and details of treatment. Animal models of antimicrobial strategies cannot reliably predict clinical efficacy [8], therefore clinical trials will be needed to evaluate whether the findings of these animal studies translate into clinical applications. This will likely be a labor-intensive and time-consuming task, but it has the potential to substantially improve management of periprosthetic infections and reduce the enormous morbidity and cost associated with these difficult to treat complications [6].

References


