Electrically Conductive Catheter Inhibits Bacterial Colonization

Hayet Amalou, MD, Ayele H. Negussie, MSc, Ashish Ranjan, PhD, Lucy Chow, MD, Sheng Xu, PhD, Craig Kroeger, BS, Ziv Neeman, MD, Naomi P. O'Grady, MD, and Bradford J. Wood, MD

ABSTRACT

Purpose: To design, prototype, and assess a custom vascular access catheter for its ability to inhibit bacterial colonization in vitro and to optimize electric parameters for efficacy and safe translation.

Materials and Methods: A vascular access catheter with conductive elements was designed and custom fabricated with two electrodes at the tip, separated by a nonconductive segment. The catheter was colonized with *Staphylococcus aureus* and incubated at predetermined current levels (4–8 μA) and durations (4–24 h). Catheters were compared using bacterial counts and scanning electron microscopy (SEM).

Results: Bacteria colony-forming units were reduced significantly ($P < .05$) by > 90% (91.7%–100%) in all uninterrupted treatment arms that included electric current (4 μA or 8 μA) of at least 8 hours' duration. Qualitative analysis using SEM revealed that the treated catheter exposed to electric current had markedly less bacteria compared with the untreated catheter.

Conclusions: This catheter with conductive elements inhibits bacterial colonization in vitro when very small electric current (4–8 μA) is applied across the tip for 8–24 hours. In vivo validation is requisite to future translation to the clinical setting.

ABBREVIATIONS

CFU = colony-forming unit, CRBSI = catheter-related bloodstream infection, DC = direct current, LB = Luria Bertani, PBS = phosphate-buffered saline, SEM = scanning electron microscopy

Central venous catheters can be associated with dangerous and costly complications, including catheter-related bloodstream infections (CRBSIs) (1). Central venous catheters are widely implanted; > 5 million catheters are in use annually in the United States (2). The lethal effects of electric current and electrochemical potentials to microorganisms have been documented for many decades (3–7). However, clinical applications remain unexplored because of absence of patient-compatible devices with integrated power sources and lack of knowledge about the safe electric parameters (duration and current) to avoid arrhythmias while maintaining bactericidal effects.

CRBSIs are often caused by coagulase-negative *Staphylococcus aureus* and enterococci, among other organisms (8). A major hurdle in confronting this infectious disease is the formation of a protective matrix or biofilm on the central venous catheter (9). These biofilms promote a community of microbes embedded in an adhesive glycopolymeric matrix and are an adapted survival mechanism to change the interaction dynamics with antibiotics and challenge host defense mechanisms (10). The biofilms are formed on the surface of the catheter by the reversible adherence of bacterial colonies that eventually adhere irreversibly by binding to the catheter surface using exopolysaccharide glycocalyx polymers and forming more stable biofilms (11). These glycocalyx polymers are produced by the microorganisms themselves and serve as an adhesive protective "force field" for the bacteria, consequently

From the Center for Interventional Oncology (H.A., A.H.N., A.R., L.C., S.X., Z.N., B.J.W.), Clinical Center and National Cancer Institute, and Critical Care Medicine Department (N.P.O.), Clinical Center, National Institutes of Health, Building 10, MSC 1182, Bethesda, MD 20892-1182; VitalDyne, Inc (C.K.), Cokato, Minnesota; and Radiological Associates (Z.N.), Philadelphia, Pennsylvania. Received September 25, 2013; final revision received and accepted January 24, 2014. **Address correspondence to** B.J.W.; E-mail: bwood@nih.gov

C.K. receives a salary from VitalDyne, Inc. None of the other authors have identified a conflict of interest.

J Vasc Interv Radiol 2014; 25:797–802

http://dx.doi.org/10.1016/j.jvir.2014.01.032

reducing the therapeutic effect of antibiotics (10,12). Antibiotic therapy typically reverses the symptoms caused by planktonic cells released from the biofilm but fails to eliminate the sequestered biofilm, isolated from usual treatments. For this reason, biofilm infections typically show recurring symptoms, despite cycles of antibiotic therapy. Even in individuals with excellent cellular and humoral immune reactions, biofilm infections are rarely resolved by host defense mechanisms. However, biofilm formation may be prevented by various strategies other than the use of antibiotic therapy.

Historically, CRBSIs have been a significant public health problem as the thirteenth leading cause of death in the United States with an estimated total annual incidence of 250,000 cases (13,14). The cost for CRBSIs was estimated as > $56,000 per incidence (15), indicating the broad economic impact. Device strategies that could reduce the incidence of CRBSIs should be inexpensive, should be easy to implement, and should have an impact on CRBSIs across broad groups of patients.

In this study, the effects of electric current on bacterial adherence and growth on a catheter surface were investigated by applying low-amperage (4–8 μA) direct current (DC). Leakage of electric current in cardiac ablation catheters should remain < 10 μA to avoid arrhythmias. This level of current is used by electrophysiology device manufacturers as a safety threshold (16). The effect of the duration of DC exposure on catheter colonization was also determined.

MATERIALS AND METHODS

Catheter

Custom sterile electric conducting catheters were designed and fabricated (VitalDyne, Inc, Cokato, Minnesota) with conductive elements from the hub to internal electrodes near the distal tip. The main shaft of the catheter is insulated with polyether block amide copolymer (Pebax; Arkema, Cary, North Carolina) with a negative charged 4-mm-long electrode ring 45 mm proximal to the tip and a positive charged 4-mm electrode ring 3 mm proximal to the distal tip, with an uninsulated conductive coating along 32 mm of the 40-mm space between the negative and positive electrodes. Electrode rings were made of platinum iridium alloy, with partially intervening conductive coating in between rings. This forces DC to be externalized along the 8-mm segment without conductive coating between the electrode rings. Although not specifically verified, this current should also travel along the thin layer of blood or saline contacting the surface of the catheter because there are not conductive elements at that segment. The conductive elements receive predetermined current on connection with a voltage generator and an ammeter that measure DC.

Bacterial Culture and In Vitro Infection Model

Catheter infection was created with live *S. aureus.* The *S. aureus* used was a virulent capsular serotype 8 pathogen. Before each treatment, *S. aureus* was cultured overnight in 10 mL of Luria Bertani (LB) broth (KD Medical Inc, Columbia, Maryland) at 37°C in ambient air overnight with shaking. A one-compartment in vitro infection model was established (**Fig 1a–c**). Briefly, 800 mL of LB broth was added into nine independent presterilized canisters (Cardinal Health, Mannford, Oklahoma) at 37°C. Next, a conducting catheter tip sterilized with ethylene oxide was inserted into each canister and shaken for a predetermined time (4, 8, or 24 hours) at 37°C while connected to stable electric current at predetermined levels (**Fig 1a**). The inserted catheters were connected to a two-channel current generator DC power supply (model 1761; BK Precision, Yorba Linda, California) supplying no current, 4 μA DC, or 8 μA DC monitored with a multimeter (model 5491A 50,000 count True RMS Bench Digital Multimeter; BK Precision). Control catheters (n = 3) were treated identically but without electric current.

Bacterial Inoculation and Incubation—Experimental Design

After securing the conducting catheter into the canister and obtaining a stable DC reading (0, 4 μA, or 8 μA), the canisters were placed on a temperature-controlled incubator shaker (MaxQ 4000; Thermo Scientific, Waltham, Massachusetts). Subsequently, the culture was inoculated with 1 mL of standardized inocula (1,000 colony-forming units [CFU]/mL) of *S. aureus* prepared in LB broth. Current treatments were performed as shown in the **Table**.

Quantitative Analysis of Treatment Effect

At the end of the treatment, each catheter from various treatment groups (**Table**) was withdrawn from the canister, gently rinsed with sterile phosphate-buffered saline (PBS; Life Technologies, Carlsbad, California), and placed in a 15-mL tube containing 7 mL of PBS. The tube was placed in a water bath sonicator (5510 Branson ultrasonic cleaner; Branson Ultrasonics Corporation, Danbury, Connecticut) for a total of five times each for 5 seconds of exposure time to detach adhered bacteria from the conducting catheter. Dilutions were made (up to 10^5) in PBS, and samples were plated on LB plates and incubated overnight at 37°C. CFU per milliliter in the tube washings were determined by manual counting after adjustment for dilution to yield the CFU/mL values.

Qualitative Analysis of Treatment Effect by Scanning Electron Microscopy

Two catheters were inoculated and incubated as previously described and studied solely for the purpose of