

Antimicrobial efficacy of the Clave[®] Connector using silver-saturated fluid path elements

BACKGROUND

The CDC estimates approximately 250,000 incidents of Catheter Related Bloodstream Infections (CRBSIs) occur annually in the United States.¹ Although the attributable mortality due to CRBSIs is not clear, these infections have been associated with higher costs, mortality rates, and number of hospital days.^{1,2} Microbial ingress is among the circumstances that risk the safe use of catheters. The Centers for Medicare & Medicaid Services (CMS) recently identified CRBSI (also defined as “Vascular Access Device Related Infection”) as one of the listed preventable medical errors. As a result, CMS ruled the treatment of CRBSI would no longer qualify for reimbursement in the 2009 fiscal year.

The Antimicrobial Clave is a mechanically and microbiologically closed needlefree connector that permits access to the catheter via use of a luer lock connection. Additionally, the Antimicrobial Clave enhances the clinically-proven needlefree technology of the Clave needlefree connector with the integration of an antimicrobial ionic silver additive to improve the barrier against microbial ingress. The Antimicrobial Clave was developed to reduce bacterial contamination on the swabbing surface and in the fluid path, both of which are major portals of entry for bacteria.

In an effort to establish guidelines for the efficacy of antimicrobial medical devices, the U.S. Food and Drug Administration (FDA) published the Premarket Notification [510(k)] Submissions for Medical Devices that Include Antimicrobial Agents (2007).³ It was determined that efficacy testing must be done on a finished device in a simulated use model. In response, ICU Medical independently contracted with AAIPharma of Wilmington, NC, to perform the required testing. The results are reported herein.

PURPOSE

Intravenous (IV) therapy is the primary route for therapeutic regimens in the acute care setting. Nearly all hospitalized patients have some type of vascular access device inserted to support their treatment. As reliance on the IV pathway has increased, the potential for accidental needlestick injuries has led to the creation of luer-activated needlefree connectors. These devices are used to connect catheters, administration sets, and/or syringes to deliver IV therapy. Unfortunately, placement of a vascular access device increases the risk of a bloodstream infection. In fact, approximately 87 percent of bloodstream infections are associated with the presence of some type of intravascular device.⁴ There are two primary portals for bacterial ingress into the bloodstream through a catheter: the first is the insertion site, and the second is the hub, which is used to administer fluids and medications. The need to effectively prevent bacterial ingress through the needlefree connector is paramount in helping to prevent bloodstream infection.

In compliance with FDA guidance, antimicrobial efficacy testing must be conducted on a finished antimicrobial device. The intent of the study is to demonstrate that the antimicrobial device will act as a barrier to intraluminal bacterial contamination under normal use. Development of the methods and protocols in this study were based on the 2007 FDA guidance for medical devices that contain antimicrobial agents. This model was selected to demonstrate the durability and efficacy of the antimicrobial agent for the useful life of the device.

1. Blot SI, Depuydt P, Annemans L, et al. Clinical and economic outcomes in critically ill patients with nosocomial catheter-related bloodstream infections. *Clin Infect Dis* 2005;41:1591-1598.

2. Centers for Disease Control and Prevention. Reduction in central line-associated bloodstream infections among patients in intensive care units—Pennsylvania, April 2001–March 2005. *MMWR Morb Mortal Wkly Rep* 2005;54:1013-1016.

3. Guidance for Industry and FDA Staff: Premarket Notification [510(k)] Submissions for Medical Devices that Include Antimicrobial Agents. 2007.

4. Ryder, M. Catheter-related infections: It's all about biofilm. *Topics Adv Pract Nurse Journal*. 2005 [cited 2006 Sept 11]; 5(3). Available www.medscape.com/viewarticle/508109.

MATERIALS AND METHODS

In order to identify the antimicrobial agent that provided the greatest efficacy and least risk, an exhaustive development program was completed and a method of manufacturing was designed to ensure proper release and distribution of the agent. This research determined the following attributes were required of the antimicrobial agent:

- › The agent must be widely accepted in clinical practice and have no measurable incidence of adverse reactions in patients.
- › The agent must be integral to the componentry and not an add-on or coating that has the risk of wearing off.
- › The agent must demonstrate clinical efficacy of greater than a 4-log kill factor for gram negative and gram positive bacteria.
- › The agent’s efficacy must be established for a 96-hour period, in accordance with CDC guidelines, when subjected to a simulated use model.

All components that have communication with the fluid path of the Clave were considered in the test, including the internal blunt cannula and split septum. Two compatible formulations of ionic silver were selected, and a protocol for integration into the materials of the split septum and the internal blunt cannula was developed. The four organisms used in the testing were:

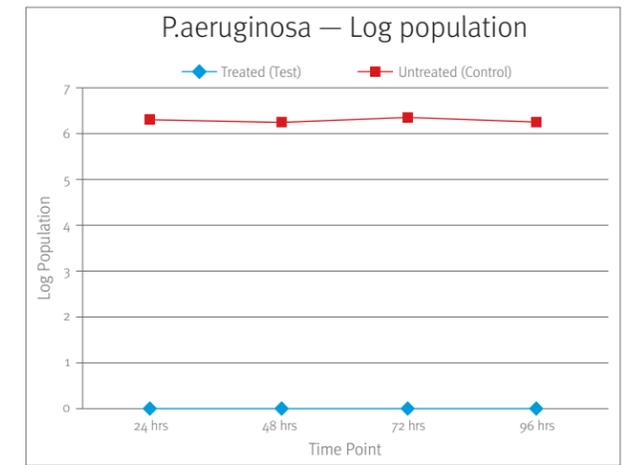
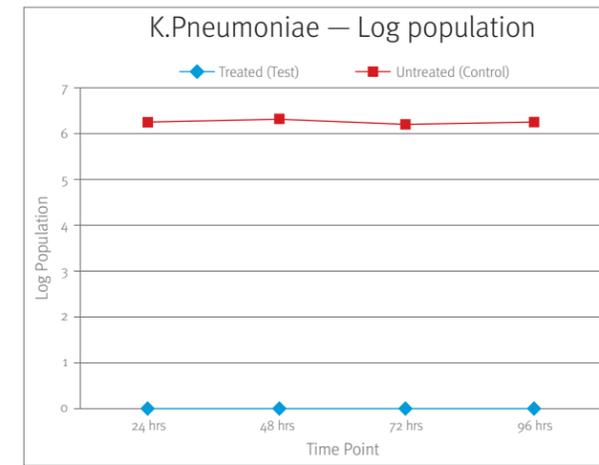
- › Staphylococcus aureus (ATCC #6538)
- › Klebsiella pneumoniae (ATCC #4352)
- › Staphylococcus epidermidis (ATCC #35984)
- › Pseudomonas aeruginosa (ATCC #9027)

For a 96-hour period, the fluid path of each device was inoculated with a 5-log concentration of the specified organism. Total bacterial counts were measured at four unique time points over the 96-hour period in order to demonstrate the durability and efficacy of the antimicrobial agent for the useful life of the device.

Antimicrobial efficacy was measured in terms of total log reduction in bacterial counts. For each bacterial model, Antimicrobial Claves were used as test devices and standard Claves were used as control devices. The bacterial reduction was calculated by comparing the inoculated count, to the number of bacteria recovered from the study devices at various time points.

RESULTS

The Antimicrobial Clave demonstrated a significant reduction in total bacteria for all four bacterial strains. In addition, the device proved capable of providing a minimum 4-log kill factor, or 99.99% efficacy, against all four strains of bacteria at various time points. The following charts show the antimicrobial efficacy of the Antimicrobial Clave as compared to the standard Clave, for each of the test microorganisms over time.



CONCLUSIONS

In all cases, the Antimicrobial Clave was effective at significantly reducing the number of bacteria for an extended 96-hour use life. The proprietary ionic silver formulation and mode of integration into the finished device was proven to be effective under simulated extreme-use conditions. While the internal fluid path design and proper adherence to infection control protocols remain important factors in limiting CRBSI, the Antimicrobial Clave may be considered an effective tool in the prevention of intraluminal bacteria colonization.

