

The Antimicrobial Effects of Silver and Chlorhexidine Added to a Luer Access Device

Todd Meyer Ph.D., Ben Luchsinger Ph.D., Melissa Kelsey

Bacterin International, Inc., 664 Cruiser Lane, Belgrade, MT 59714

Purpose

The use of luer access needleless connectors (NC), while providing pronounced advantages in terms of lowering the incidence of needle-stick injuries, has also been accompanied by an increase in catheter-related bloodstream infections (CRBSI).^{1,2} These nosocomial infections have been shown to be associated with microbial contamination within such devices. A potential solution to this problem as it relates to microbial contamination of the NC is to treat the entry point and fluid path of the device with antimicrobial agents.

The conventional disinfection protocol, swabbing the exterior surface of the NC with 70% alcohol, has been shown to be ineffective, allowing transmission of microorganisms into the fluid pathway in 67% of devices sampled.³ The effect of NCs on CRBSI has been investigated and shown to be associated with biofilm development.⁴ Microorganisms can evade the barrier protection provided by the septum, colonize the interior of the NC, multiply and form a biofilm.

We report herein microbiological testing of a mechanical valve NC containing two antimicrobial agents, silver ions and chlorhexidine, applied to the septum of a commercially available mechanical valve NC. Additionally, silver has been applied to the interior fluid path of the device. The objective of this study was to establish whether such an application of antimicrobial agents to the septum would show antimicrobial efficacy under *in vitro* conditions.

Method

InVision-Plus® Neutral® I.V. Connectors (RyMed Technologies, Inc., Franklin, TN) employ an elastomeric septum (labeled **●** in Figure 1b). Septa were treated with both silver ions and chlorhexidine using a proprietary method developed at Bacterin International, Inc. The interior fluid path of the device was treated with silver. Following gamma sterilization, the septa and spike body (which contains the fluid path) were subjected to antimicrobial efficacy testing.

The septa treated with silver ions and chlorhexidine and spike body containing silver were tested for antimicrobial efficacy alongside untreated control septa and spike bodies. For each test organism, 1 untreated control and 3 treated test connectors and were used.

The septa and spike bodies were tested using a solution of tryptic soy broth (TSB) in phosphate buffered saline (PBS) contaminated with approximately 10⁶ colony forming units (CFU)/mL of the following organisms: Methicillin-resistant *Staphylococcus aureus* (MRSA), *Pseudomonas aeruginosa*, *Klebsiella pneumoniae*, *Escherichia coli*, *Acinetobacter baumannii*, *Staphylococcus aureus*, *Candida albicans*, and *Staphylococcus epidermidis*. The composition of the solution was chosen so as to maintain consistent organism concentration throughout the 7 day test period; 0.25% TSB for *P. aeruginosa* and *E. coli*, and 0.5% TSB for MRSA, *K. pneumoniae*, *A. baumannii*, *S. aureus*, *C. albicans*, and *S. epidermidis*.

Test solutions were incubated at approximately 25 °C. At days 4 and 7, aliquots were removed and neutralized. Appropriate dilutions were performed, and the diluted solutions plated on 5% sheep's blood agar, incubated at 35 °C, enumerated, and log reductions calculated.

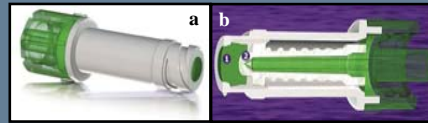


Figure 1: InVision-Plus® Neutral® I.V. Connectors (RyMed Technologies, Inc., Franklin, TN)

Organism	Log Reduction	
	Day 4	Day 7
MRSA (clinical isolate)	5.5	7.0
<i>E. coli</i> (ATCC #8739)	5.2	4.9
<i>S. aureus</i> (ATCC #6538)	4.2	4.2
<i>P. aeruginosa</i> (ATCC #9027)	4.3	4.5
<i>A. baumannii</i> (ATCC #19606)	4.5	5.4
<i>S. epidermidis</i> (clinical isolate)	4.0	6.0
<i>K. pneumoniae</i> (ATCC #4352)	5.5	5.1
<i>C. albicans</i> (ATCC #38245)	3.5	3.3

Table 1: Day 4 and Day 7 Log Reduction, Treated vs Untreated

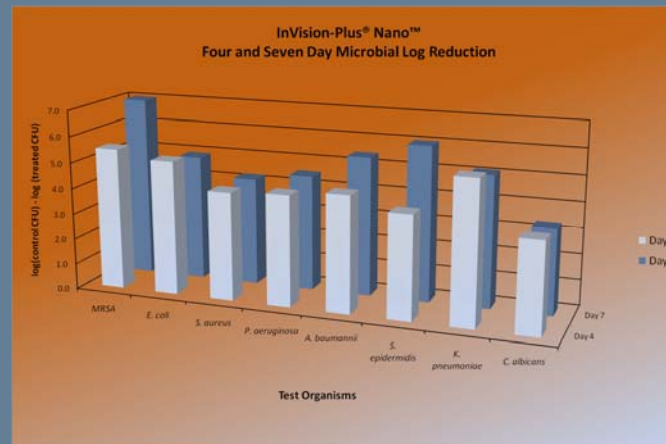


Figure 2: Day 4 and Day 7 Log Reduction, Treated vs Untreated

Results

The results are shown in Table 1 and in Figure 2 as log reduction: $\log(\text{control CFU}) - \log(\text{treated CFU})$. Day 4 and day 7 results show greater than four log reduction for all bacterial test organisms. Note that there is an increase in the log reduction of organism populations between days 4 and 7, except for *E. coli*, *S. aureus*, *C. albicans*, and *K. pneumoniae*. Microbiocidal effects against a wide range of organisms is demonstrated.

These results imply that the RyMed InVision-Plus® Nano™, which contains a septum treated with antimicrobial agents, may potentially play an important role in reducing bioburden on the septum of the device, and within the fluid pathway. The importance of this should be noted: the septum is the entry point for microorganisms into the bloodstream.

Conclusions

This study shows that application of two antimicrobial agents, silver ions and chlorhexidine, to the septum of a needleless connector, as well as the application of silver to the fluid pathway of the device results in meaningful log reductions versus untreated control devices in an *in vitro* time-kill assay. Such a reduction in bioburden on the surface of the septum and in the fluid pathway has the potential to translate into a reduction in organism counts at the distal end of the device.

Limitations

The clinical efficacy of this device has not been established. The subject device is not intended to treat existing infections, and is not intended to have any effect on contaminated infusion solutions. The antimicrobial agents on the device may not be effective against all microbial strains encountered clinically.

Disclosure Statement

This work was supported by RyMed Technologies, Inc.

References

- McDonald LC, Banerjee SN, Jarvis WR; Line-Associated Bloodstream Infections in Pediatric Intensive Care Unit Patients Associated with a Needleless Device and Intermittent Intravenous Therapy. *Infect Control Hosp Epidemiol* 1998, 19, 772.
- Jarvis W, Sheretz R, Perl T, Bradley K, Giannetta E; Increased Central Venous Catheter-Associated Bloodstream Infection Rates Temporally Associated with Changing From a Split-Septum to a Luer-Access Mechanical Valve Needleless Device: A Nationwide Outbreak? *Am J Infect Control* 2005, 33(5), e14.
- Menyhay SZ, Maki DG; Disinfection of Needleless Catheter Connectors and Access Ports with Alcohol May Not Prevent Microbial Entry: The Promise of a Novel Antiseptic-Barrier. *Infect Control Hosp Epidemiol* 2006, 27, 23.
- Donlan RM, Murga R, Bell M, Toscano CM, Carr JH, Novicki TJ, Zuckerman C, Corey LC, Miller JM; Protocol for Detection of Biofilms on Needleless Connector Attached to Central Venous Catheters. *J Clin Microbiol* 2001, 39(2), 750.