MRSA Prevention: Are Hand Hygiene Products Effective at Reducing MRSA on the Hands?

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Abstract

Background: Methicillin-resistant *Staphylococcus aureus* (MRSA) is an increasingly problematic pathogen in hospitals. The CDC recommends proper hand hygiene for prevention of MRSA, including use of alcohol-based hand sanitizer and /or washing with soap and water. However, minimal data is available on the effectiveness of common hand hygiene products at reducing MRSA on the hands.

Objectives: The objective of this study was to evaluate, using an *in vivo* handwash methodology, the effectiveness of three hand hygiene products containing different active ingredients versus MRSA. An additional objective of the study was to assess whether *in vitro* Time-Kill data are adequate predictors of *in vivo* product efficacy.

Methods: The test products were commercially available hand hygiene products: an alcohol-based hand sanitizer (ABHS) with 62% ethanol, an antibacterial handwash with 0.3% triclosan (TCS), and an antibacterial handwash with 4% chlorhexidine gluconate (CHG). MRSA (ATCC#33591) was the test organism. *In vitro* Time-Kill experiments were carried out according to ASTM E 2315 guide using a 15-second contact time. A modification of ASTM E 1174-06 was used to evaluate test product efficacy on the hands of human volunteers. Twelve volunteers evaluated each test product (1.5 ml volume) in a cross-over design. Statistical comparison of $\log_{10}$ reductions (LR) was performed using the Fisher's LSD Test ($p<0.05$).

Results: The ABHS achieved complete reduction (≥6.297 LR) of MRSA when tested with *in vitro* Time-Kill. The TCS and CHG handwashes produced a 3.11 LR and a 1.22 LR, respectively. By the *in vivo* method, the ABHS, the TCS handwash, and the CHG handwash produced LR ± standard deviations of 2.05 ±0.54, 1.93±0.35 and 1.53±0.27, respectively. The ABHS and TCS handwash were statistically equivalent, and both were significantly more effective than the CHG handwash.

Conclusions:

- *In vitro* time kill data were predictive of relative *in vivo* efficacy, but did not correlate with *in vivo* LRs; therefore, caution should be exercised when interpreting efficacy data for hand hygiene products.
- When tested using realistic product volumes, the ABHS and the TCS handwash were effective against MRSA, reducing levels on human hands by approximately 99%.
- The CHG handwash was less effective against MRSA, suggesting that CHG may not be an appropriate hand hygiene option for MRSA, particularly after a single use.

Introduction

MRSA has been a problematic pathogen in hospital environments for over 40 years[1]. MRSA is a leading cause of skin and soft tissue infections and can result in severe infections and death[2,3]. Prevention of MRSA infections and transmission is an important part of controlling this pathogen in hospitals. Prevention is of increasing importance as new strains of MRSA continue to emerge with various antimicrobial resistance patterns that make infections difficult to treat with antibiotics.

Proper hand hygiene is recommended by the CDC for prevention of MRSA transmission[4]. Washing hands with soap and water or use of an alcohol-based hand sanitizer is one of the most important interventions to help prevent the spread of infections[4]. Multiple studies have shown the effectiveness of increased hand hygiene compliance, including use of alcohol-based hand sanitizer, for reduction of MRSA transmission[5-6]. Currently most hand hygiene products are evaluated *in vitro* for MRSA activity, and *in vivo* data are limited due to the difficult nature of conducting *in vivo* studies with this organism. Existing *in vivo* MRSA data on the effectiveness of hand hygiene products indicates that the efficacy against MRSA is variable[7-8]. In addition, different strains of MRSA have variable susceptibility to biocides, and MRSA ATCC #33591 has intermediate susceptibility to common antimicrobials when compared to several clinical hospital-associated and community-associated MRSA strains[9].

The aim of this study was to determine the *in vitro* and *in vivo* effectiveness of common hand hygiene agents against a representative strain of MRSA. A secondary aim of this study is to determine whether *in vitro* data are a reasonable predictor of *in vivo* MRSA efficacy.

Additional Information

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References:

1. Barrett FF, McGehee RF, Jr., Finland M. Methicillin-resistant Staphylococcus aureus at Boston City Hospital. Bacteriologic and epidemiologic observations. N Engl J Med 1968 Aug 29;279(9):441-8.
2. Klevens, et. al. Invasive Methicillin-Resistant Staphylococcus aureus Infections in the United States. JAMA 2007 Oct 17;298(15):1763-1771.
3. Moran et al. NEJM 2006; 355:666-674.
4. Boyce J, Pittet D. Guideline for Hand Hygiene in Health-Care Settings: Recommendations of the Healthcare Infection Control Practices Advisory Committee and the HICPAC/SHEA/APIC/IDSA Hand Hygiene Task Force. 51 ed. 2002.
5. Girou E, Legrand P, Soing-Altrach S, et al. Association between hand hygiene compliance and methicillin-resistant Staphylococcus aureus prevalence in a French rehabilitation hospital. Infect Control Hosp Epidemiol 2006 Oct;27(10):1128-30.
6. MacDonald A, Dinah F, MacKenzie D, Wilson A. Performance feedback of hand hygiene, using alcohol gel as the skin decontaminant, reduces the number of inpatients newly affected by MRSA and antibiotic costs. J Hosp Infect 2004 Jan;56(1):56-63.
7. Cole G, Duran J, Fuls A, et al. The Effect of Antimicrobial Hand Washes on Methicillin Resistant Staphylococcus aureus.108th Annual Meeting of the American Society of Microbiology, Boston, MA: 2008.
8. Hernandes SE, de Mello AC, Sant'Ana JJ, et al. The Effectiveness of Alcohol Gel and Other Hand-Cleansing Agents Against Important Nosocomial Pathogens. 35 ed. 2004. p. 33-9.
9. Bondi et al. In-Vitro Susceptibility of Hospital-Acquired, Community-Acquired, and Laboratory MRSA Strains. Presented at the 2008 American Public Health Association (APHA) Conference, San Diego, CA

Materials and Methods:

Test Products:

Three commercially available hand hygiene products were assessed in this study. A 62% ethanol gel hand sanitizer (PURELL® Instant Hand Sanitizer, GOJO Industries, Inc, Akron, OH), a 0.3% triclosan foam handwash (PROVON® Foaming Medicated Handwash with Moisturizers and Triclosan, GOJO Industries, Inc., Akron, OH), and a 4% CHG liquid handwash (Hibiclens Antiseptic / Antimicrobial Skin Cleanser, Mölnlycke Health Care, Norcross, GA).

***In Vitro* MRSA Time-Kill Assay:**

A challenge suspension of MRSA ATCC# 33591 was prepared to achieve a concentration of 10^9 CFU/mL. The initial population was determined by ten-fold dilutions in Butterfield's Phosphate Buffer with product neutralizers (BBP++). A 0.1mL aliquot of a challenge suspension containing 10^9 CFU/mL was transferred to a sterile test tube containing 9.9mL of test article, vortexed thoroughly and exposed for 15 seconds. 1.0mL was removed and neutralized in 9.0mL of BBP++, serially diluted at 1:10, and pour-plated in duplicate using TSA+. Plates were incubated at 35°C for 48-72 hours, or until sufficient growth was observed. A neutralization study according to ASTM E 1054-02 was conducted to ensure that the neutralizing solution BBP++ was effective. Following incubation, colonies on plates were counted manually. Counts in the range of 30-300 CFU (or those closest to that range) were used in data calculations. To calculate the $\log_{10}$ reduction, the following equation was used:

$$\text{Log}_{10}\text{ Reduction} = \text{Log}_{10}\text{ Initial Population} - \text{Log}_{10}\text{ Population After Exposure to the Test Formulation}$$

***In Vivo* MRSA Hand Wash Study:**

The study was performed according to the ASTM E1174 "Standard test method for evaluation of the effectiveness of health care personnel handwash formulations" with modification of challenge organism and the procedure used to contaminate the hands. The study was a 12 subject non-randomized cross-over design, where each subject completed the baseline evaluation, followed by use of 62% ethanol gel, 0.3% triclosan handwash, and 4% CHG handwash. A neutralization study per ASTM E 1054-02 was performed to ensure the neutralizer employed in this study was effective.

Step 1: Inoculate hands with 200 µl of MRSA (ATCC #33591) at a concentration of ~$1x10^9$ CFU / ml

Step 2: Apply ~1.5ml test product according to specified application method (skip this step for baseline calculation)

Step 3: Place powder free sterile latex glove on hand

Step 4: Add Sterile Striping Fluid with product neutralizers into glove

Step 5 Massage hand vigorously for 60 seconds

Step 6: Remove sample of glove juice

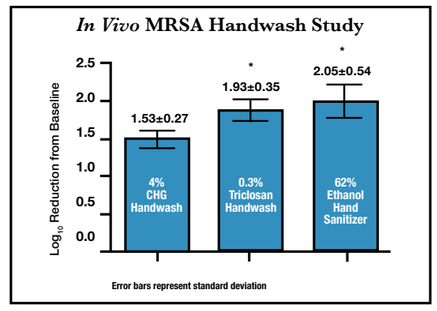
Step 7: Serially dilute in neutralizing solution, plate on Mannitol Salt Agar, grow overnight at 35°C and compare to baseline values to calculate $\log_{10}$ reductions. Statistical analysis was conducted using ANOVA ($P<0.05$).

Results:

***In Vitro* Time-Kill Assay (15-s Exposure)**

Test Product	Log_{10} Reduction
62% Ethanol Gel Hand Sanitizer	≥6.30
0.3% Triclosan Foam Handwash	3.11
4% CHG Liquid Handwash	1.22

≥ sign indicates complete kill at the limit of detection



*The $\log_{10}$ reductions from baseline for the 0.3% triclosan handwash and 62% ethanol hand sanitizer were statistically equivalent. Both were statistically superior to the 4% CHG handwash.

Conclusions:

- Using "real-world" product volumes, the 62% ethanol gel hand sanitizer achieved complete reduction of MRSA by in vitro Time-Kill and a ≥2 log10 reduction from baseline in the in vivo hand wash study. Therefore, use of alcohol-based hand sanitizers for prevention of MRSA transmission is supported.
- A well-formulated triclosan handwash was equivalent to the 62% ethanol hand sanitizer in the *in vivo* hand wash study and is therefore an effective option for reduction of MRSA on the hands.
- The 4% CHG liquid handwash was the least effective product tested, with the lowest $\log_{10}$ reduction *in vitro* and significantly less efficacy *in vivo*. Therefore, CHG products may not be appropriate for reducing MRSA on the hands.
- *In vitro* Time-Kill data was not predictive of *in vivo* log reductions, and should be interpreted cautiously. However, Time-Kill was useful for predicting the relative product efficacy of hand hygiene products.