



Efficacy of Skin and Nasal Povidone-Iodine Preparation and Iodine-containing Formulations in Treating MRSA Colonization of Ex Vivo Mucosal Tissue Model

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Abstract

Background: Mupirocin decolonization of nasal *Staphylococcus aureus* prior to surgery decreases surgical site infections (SSIs), however, treatment is 5 days and resistance may occur. 3M™ Company povidone-iodine (PVP-I) based Skin and Nasal Antiseptic (SNP) has rapid, broad spectrum antibacterial activity and resistance is low. Nasal povidone-iodine solution may be considered as an alternative to mupirocin in a multifaceted approach to reduce SSI (1). The aim of this study was to determine the efficacy of 3M SNP and other PVP-I containing formulations (Betadine® Solution and Clorox Healthcare™ Nasal Antiseptic Swabs) in treating methicillin-resistant *S. aureus* (MRSA) colonization of ex vivo mucosal tissue.

Methods: Explants of porcine vaginal mucosa (PVM, 5 mm, full-thickness squamous epithelium) were infected with MRSA USA300 LAC strain or high-level mupirocin-resistant isolates (476 or 920) (1×10^6 CFU/explants). Following 2h infection, explants were treated with 3M SNP, Clorox Healthcare Nasal Antiseptic or Betadine Solution for 1 h or left untreated. Explants were washed with PBS + 2% mucin to mimic mucociliary clearance and incubated at 37°C for 1 h, 6 h or 24 h. Bacteria were enumerated by transferring explants to neutralization broth, vortex mixing and plating. Data presented are $M \pm SEM$, $N \geq 5$, $n=3$.

Results: Treatment with 3M SNP, Clorox Healthcare Nasal or Betadine Solution resulted in a $5.8 \pm 0.26 \log_{10}$, $4.1 \pm 0.42 \log_{10}$, or $4.8 \pm 0.41 \log_{10}$ reduction in MRSA (LAC and MRSA mupirocin-resistant isolates, $n=2$) (CFU/explants), respectively. All treatments were significantly different from untreated control 1 h post-wash. 3M SNP had significant persistence at 6 h ($6.6 \pm 0.47 \log_{10}$ reduction) and at 24 h. Whereas Clorox Healthcare Nasal and Betadine Solution were less effective at 6 h ($3.5 \pm 0.4 \log_{10}$ and $4.1 \pm 0.60 \log_{10}$ reduction). By 24 h, regrowth was observed in the Clorox Healthcare Nasal Antiseptic and Betadine Solution treatment groups. The persistent antimicrobial effect of 3M SNP at 24 h was significantly better than that of all other treatments ($6.9 \pm 0.41 \log_{10}$ versus Clorox Healthcare Nasal's $2.4 \pm 0.51 \log_{10}$ or Betadine Solution's $1.9 \pm 0.37 \log_{10}$), difference from untreated controls.

Conclusion: PVP-I formulations significantly reduce MRSA colonization of ex vivo mucosal tissue at 1 h; however, 3M SNP was persistent and superior to Clorox Healthcare Nasal Antiseptic and Betadine Solution for reducing MRSA (including MRSA high-level mupirocin-resistant isolates) burden over 24 h.

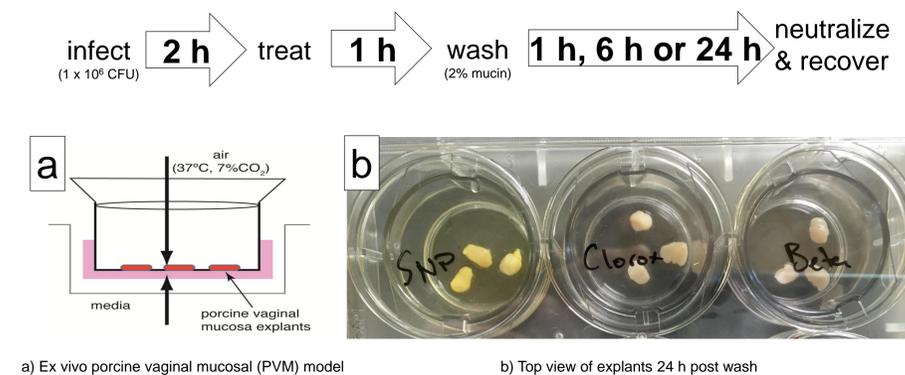
Introduction

- *S. aureus* is a major community and nosocomial pathogen.
- *S. aureus* nasal carriage is a risk factor for infection.
- Mupirocin based treatments may lead to antibiotic resistance.
- Bacteria have not been shown to develop resistance to PVP-I.
- PVP-I containing products evaluated in study:
 - 3M Skin and Nasal Antiseptic (Povidone-iodine solution 5% w/v [0.5% available iodine] USP)
 - Clorox Healthcare Nasal Antiseptic Swabs, Povidone-iodine USP 10%
 - Betadine Solution, 10% Povidone-iodine
- Testing product efficacy on an ex vivo PVM model is translational in nature (2).

The objective of this study was to determine the anti-staphylococcal efficacy (treatment and prevention) of 3M Skin and Nasal Antiseptic in comparison to Clorox Healthcare Nasal Antiseptic and Betadine Solution.

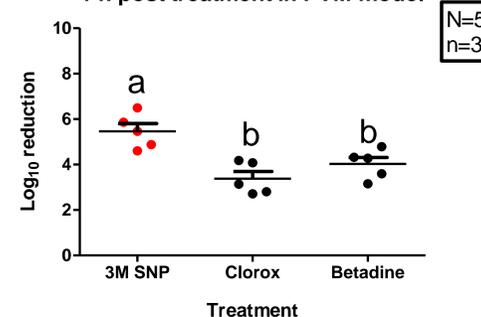
Methods & Results

General methods: Explants of normal porcine vaginal mucosa (PVM, 5 mm, full-thickness squamous epithelium) were infected with methicillin-resistant *S. aureus* (USA300 LAC) or high-level mupirocin-resistant (MIC $\geq 1,024 \mu\text{g/ml}$) MRSA (476 and 920) isolates. Following infection, explants were treated with 3M Skin and Nasal Antiseptic, Clorox Healthcare Nasal Antiseptic, Betadine Solution, or untreated (controls). Following treatment, explants were washed in sterile PBS containing 2% w/v mucin, to mimic mucociliary clearance. Explants were further incubated for 1 h, 6 h or 24 h. Bacteria were enumerated by transferring explants to 2x DE broth for neutralization, vortex mixing then plating onto Tryptic Soy with 5% sheep's blood neat or serially diluted in PBS.

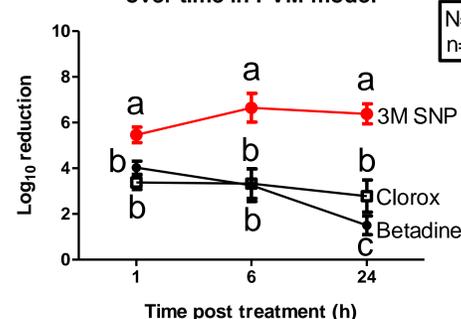


3M SNP exhibited persistent antiseptic activity throughout the course of the experiments (up to 24 h).

MRSA (LAC) log reduction from growth control 1 h post treatment in PVM model



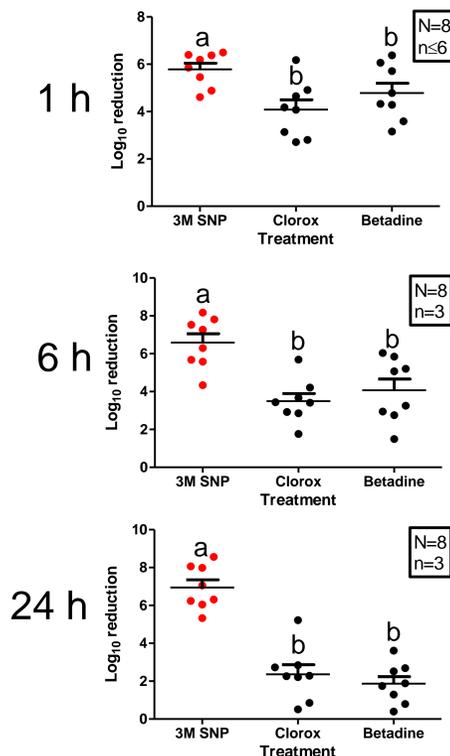
MRSA (LAC) log reduction from growth control over time in PVM model



Data presented are means and standard errors of the means (SEMs). Analysis of variance (ANOVA) followed by Bonferroni's multiple comparison posttest were performed using the GraphPad PRISM software (GraphPad Software, Inc., La Jolla, CA). Treatments not sharing a letter are significantly different. $p \leq 0.05$

Results (continued)

Efficacy of 3M SNP, Clorox Nasal Antiseptic, and Betadine against USA300 LAC and high-level mupirocin-resistant MRSA isolates ($n=2$)



Data presented are means and standard errors of the means (SEMs). Analysis of variance (ANOVA) followed by Bonferroni's multiple comparison posttest were performed using the GraphPad PRISM software (GraphPad Software, Inc., La Jolla, CA). Treatments not sharing a letter are significantly different. $p \leq 0.05$

Summary

- 3M SNP was significantly more effective than Clorox and Betadine against MRSA (LAC) alone and high-level mupirocin-resistant MRSA isolates ($n=2$) at 1 h treatment period in the ex vivo PVM model.
- 3M SNP exhibited persistent antiseptic activity throughout the course of the experiments (up to 24 h) and was significantly different than other treatment groups at 6 h and 24 h.
- There was no significant log CFU reduction difference between Betadine and Clorox against the MRSA (LAC) and MRSA/high-level mupirocin-resistant isolates.

Conclusion

- 3M SNP was persistent and superior to Clorox Healthcare Nasal Antiseptic and Betadine Solution for reducing MRSA (including MRSA high-level mupirocin-resistant isolates) burden over 24 h.

References

- (1) Phillips M, Rosenberg A, Shopsis B, et al. Preventing surgical site infections: A randomized, open-label trial of nasal mupirocin ointment and nasal povidone-iodine solution. *Infect Control Hosp Epidemiol* 2014;35(7):826-832.
- (2) Anderson MJ, David ML, Scholz M, Bull SJ, Morse D, Hulse-Stevens M, et al. Efficacy of Skin and Nasal Povidone-Iodine Preparation against Mupirocin-Resistant Methicillin-Resistant *Staphylococcus aureus* and *S. aureus* within the Anterior Nares. *Antimicrob Agents Chemother*. 2015;59:2765-73.

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