Reduction of *Staphylococcus aureus* Carriage by Non-Antibiotic NOZIN® Nasal Sanitizer® Antiseptic

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ABSTRACT

Background: Healthcare professionals (HCP) that are nasal *S. aureus* carriers may be a source of transmission of this organism to their patients. Antibiotics such as mupirocin have been used successfully to control nasal colonization in pre-surgical patients, but this practice is unlikely to be useful for HCP with constant exposure to *S. aureus* and is likely to lead to antibiotic resistance. In preliminary clinical testing, NOZIN® Nasal Sanitizer® has been shown to reduce harmful microbes.

Methods: We conducted a double-blinded treatment effectiveness pilot study of HCP with culture-proven nasal *S. aureus* colonization within the previous 10 days. HCP with positive cultures were treated with NOZIN® or placebo at 0 hour, 4 hours, and 8 hours. Nasal vestibular samples were collected at time 0 prior to nasal topical application and at 10 hours; total bacterial counts and *S. aureus* bacterial counts were determined.

Results: Of the 357 participants screened, 78(20.2%) participants tested positive for *S. aureus*. A total of 39 participants were enrolled in the treatment phase of the study with 20 treated with NOZIN® and 19 receiving placebo. Three times daily use of the NOZIN® Nasal Sanitizer® antiseptic significantly reduced the number of nasal bacterial colonies from 1200±379 at baseline to 167±70 ($P < 0.001$) at the end of the 10-hour study period. Furthermore, NOZIN® Nasal Sanitizer® reduced the number of *S. aureus* colonies 756±336 at baseline to 30±12 ($P < 0.001$). Nineteen (95%) of out twenty subjects showed significant reduction ($p<0.05$) in *S. aureus*, and all 20 (100%) subjects showed significant ($p<0.05$) reduction in nasal bacteria. There were no adverse events with the use of NOZIN® Nasal Sanitizer® antiseptic.

Conclusions: NOZIN® Nasal Sanitizer® was found to be very effective in reducing *S. aureus* and nasal bacterial carriage. A broader clinical trial should be conducted to determine if reducing HCP *S aureus* nasal carriage will reduce patient infections.

INTRODUCTION

Current understanding of nasal *S. aureus* colonization indicates that approximately 20-40% of healthy individuals within the continental U.S. may be either persistent or intermittent carriers. Even intermittent carriers can sustain sub-clinical carriage for 4-14 days putting them in a position to increase risk for *S. aureus* infection in themselves or others with whom they come in contact. Studies of nasal *S. aureus* in HCPs have shown levels of colonization similar to those of the general population, with the proportion of MRSA in carriers being similar (5.6%) in both. It has been suggested that in colonized HCPs, self-infection, cross-transmission to patients, and introduction of the pathogen into their communities are likely possibilities.

While antibiotics such as mupirocin have been used successfully to control nasal colonization in pre-surgical patients, this practice is unlikely to be useful for HCP with constant exposure to *S. aureus* and is likely to lead to antibiotic resistance. In contrast, a broad spectrum antiseptic agent such as ethanol should reduce bacterial colonization with development of resistance being unlikely. Among HCPs, a nasal antiseptic, along with hand sanitation, could be part of a regular regimen of professional preventive hygiene in the workplace. In addition, a preparation formulated to provide persistence of antimicrobial activity that could be applied periodically during the course of the workday would minimize the burden of its use.

METHODS

Study Protocol: see Figure 1

Preparation and Application of the Test and Control Agents: NOZIN® Nasal Sanitizer® (Global Life Technologies Corp., Chevy Chase, Maryland) is a commercially available, non-prescription product that combines 70% ethanol, benzalkonium chloride, and natural oils. Sterile saline was used as the sham treatment. Antiseptic or sham was applied by rotating a saturated sterile nylon swab around the inside surfaces of both vestibules. Application of the sham controlled for potential mechanical effects of the application process itself.

Sample Collection and Analysis: Nasal samples for both screening and study sample collection were obtained using BD ESwab Collection Kits (Becton, Dickinson & Co., Sparks, MD). For screening, nasal swabs were inoculated onto BBL™ CHROMagar™ *Staph aureus* plates (Becton, Dickinson & Co.) and incubated at 35ºC for 24 hrs; mauve-colored colonies were identified as *S. aureus* by Gram stain, catalase and latex agglutination testing. For evaluation of treatment samples, duplicate 75 ul aliquots of neat and 10-fold dilutions were inoculated onto plates of BBL™ CHROMagar™ *Staph aureus* and tryptic soy agar with 5% sheep blood (TSA). *S. aureus* and total bacterial CFUs were counted at 24 hours and 48 hours using photographs of the plates taken at those times. *S. aureus* and total bacterial CFUs were derived from pairs of plates on which identical aliquots of each nasal sample were cultured. In the event that either neat colony density was too high to allow accurate counting, the pair of 10-fold dilution plates for that subject was used and CFUs were multiplied by 10. All data from subjects whose baseline samples grew fewer than 5 mauve colonies on the CHROMagar plates were excluded from analysis.

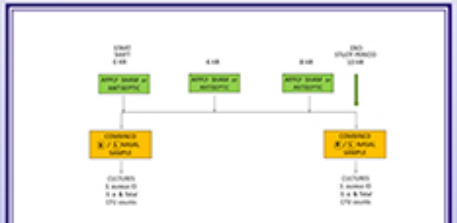

Figure 1. Schematic of the study protocol. Three applications of sham or antiseptic preparation were made at 4-hr intervals during the workday to both nasal vestibules of subjects randomly assigned to one of the two treatment groups. Combined nasal swab samples from both vestibules were collected pre- and post-treatment, at 0 and 10 hrs, to assess changes in nasal vestibular *S. aureus* and total bacterial CFU counts.

TABLE 1. Characteristics of the Screened HCP Study Participants

Characteristic	No. (%) (n = 357)	*S. aureus* Positive No. (%)	OR [95% CI]*	P*
Mean Age	42.8 years			
Total Screened	357 (100)	78 (20.2)		
Female	329 (85.0)	65 (19.8)	Ref	-
Male	58 (15.0)	13 (22.4)	1.17 (0.60 – 2.3)	0.77
Position Title				
RN	179 (46.3)	42 (24.3)	Ref	-
PCT/ORA	50 (12.9)	8 (16.0)	0.54 (0.23 – 1.22)	0.19
MD/PA/NP/CRNA	35 (9.0)	7 (20.0)	0.70 (0.29 – 1.71)	0.57
Other	123 (31.8)	16 (13.0)	0.42 (0.23 – 0.78)	0.65
Work Location				
Floors	212 (54.9)	41 (19.3)	Ref	-
OR	132 (34.1)	24 (18.2)	1.14 (0.65 – 2.00)	0.76
Other	42 (10.9)	13 (31.0)	1.11 (0.55 – 2.23)	0.92
Children 6 mos – 11 yrs	102 (26.4)	20 (19.6)	0.96 (0.54 – 1.68)	0.99
Dept[a]	180 (46.5)	37 (20.6)	1.05 (0.64 – 1.72)	0.96
Cath[b]	67 (17.3)	11 (22.4)	1.18 (0.62 – 2.23)	0.74

HCP = Health Care Professional, OR = odds ratio, CI = confidence interval, RN = registered nurse, PCT = patient care technician, ORA = operating room assistant, MD = physician, PA = physician assistant, CRNA = certified registered nurse anesthetist, OR = operating room, Ref = reference group.
* Calculated using the indicated reference group and comparing the *S. aureus* positive population to the *S. aureus* negative population.
† Calculated using the indicated reference group or the corresponding negative characteristic group and comparing the *S. aureus* positive population to the *S. aureus* negative population. The X^2 test was used.

TABLE 2. Comparison of Characteristics of Treatment Groups in *S. aureus* -positive HCPs

Characteristic	Control	Antiseptic
Total Subjects	19	20
Mean Age Years (range)	35.4 (26-67)	34.5 (26-64)
Baseline colonization		
S. aureus CFU ± SD	562 ± 1113	756 ± 1512
Total bacterial CFU ± SD	1280 ± 1718	1200 ± 1694
Female	14	20
Male	5	0
Occupation		
RN	10	15
PCT/ORA	1	2
MD/PA/NP/CRNA	5	0
Other	3	3
Location		
Floors	14	14
OR	1	4
Other	4	2

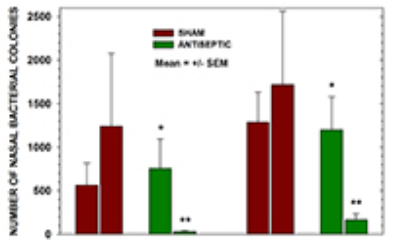

Figure 2. Nasal vestibular bacterial colonization in baseline (PRE) and post treatment samples. Numbers of CFUs in identical samples plated onto CHROMagar SA and TSA blood agar plates for assessment of *S. aureus* and total bacterial CFUs pre and post treatment.
* indicates no significant difference from the baseline value in the corresponding sham-treated group.
** indicates significantly different ($p < 0.001$) from the baseline (PRE) value.

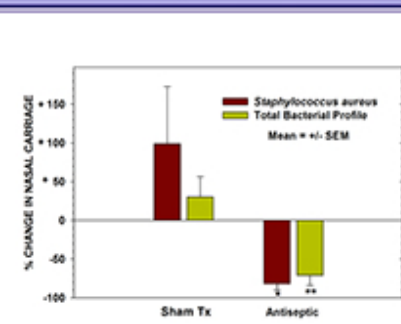

Figure 3. Comparison of the effects of sham and antiseptic application procedures on bacterial colonization during the study period
Mean percent changes in bacterial carriage resulting from the process of applying saline versus an active antiseptic.
* indicates significant difference ($p < 0.001$) from *S. aureus* in the sham-treated subjects.
** indicates significant difference ($p < 0.001$) from total bacterial profile in the sham-treated subjects.

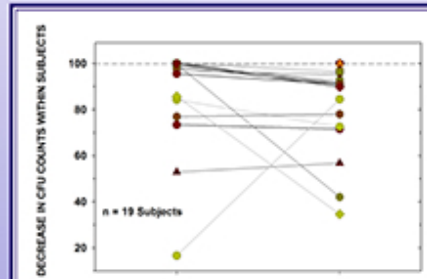

Figure 4. Concurrence in target-specific antiseptic effects within individual subjects. Comparison between percent reductions in *S. aureus* and total bacteria CFUs in individual antiseptic-treated subjects based on identical nasal vestibular samples.

SUMMARY

1. Application of an alcohol–based, non-antibiotic nasal antiseptic demonstrated effectiveness in markedly reducing *S. aureus* colonization during the course of a 10 hour workday in HCPs.
2. Treatment resulted in similar reductions in total nasal bacterial carriage.
3. If properly formulated to eliminate nasal irritation and dryness, alcohol-based antiseptics can be well-tolerated in a multiple application daily regimen.

CONCLUSIONS

1. Alcoho–based nasal antiseptics may provide an adjunct or alternative to the use of antibiotic preparations for the control of nasal colonization by potentially pathogenic bacteria, such as *S. aureus*.
2. The daily use of nasal antiseptics by HCPs, as well as their patients, may offer an important new paradigm for personal protection and infection control in the health care setting.