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Major article

Reduction of nasal *Staphylococcus aureus* carriage in health care professionals by treatment with a nonantibiotic, alcohol-based nasal antiseptic

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Background: Antibiotics used to reduce nasal colonization by *Staphylococcus aureus* in patients before admission are inappropriate for carriage reduction on a regular basis within a hospital community. Effective nonantibiotic alternatives for daily use in the nares will allow reduction of this bacterial source to be addressed.

Methods: Our study tested the effectiveness of a nonantibiotic, alcohol-based antiseptic in reducing nasal bacterial carriage in health care professionals (HCPs) at an urban hospital center. HCPs testing positive for vestibular *S aureus* colonization were treated 3 times during the day with topical antiseptic or control preparations. Nasal *S aureus* and total bacterial colonization levels were determined before and at the end of a 10-hour workday.

Results: Seventy-eight of 387 HCPs screened (20.2%) tested positive for *S aureus* infection. Of 39 subjects who tested positive for *S aureus* infection who completed the study, 20 received antiseptic and 19 received placebo treatment. Antiseptic treatment reduced *S aureus* colony forming units from baseline by 99% (median) and 82% (mean) ($P < .001$). Total bacterial colony forming units were reduced by 91% (median) and 71% (mean) ($P < .001$).

Conclusions: Nasal application of a nonantibiotic, alcohol-based antiseptic was effective in reducing *S aureus* and total bacterial carriage, suggesting the usefulness of this approach as a safe, effective, and convenient alternative to antibiotic treatment.

Although estimates vary, studies indicate that between 20% and 40% of healthy individuals within the continental United States exhibit nasal vestibular carriage of *Staphylococcus aureus*.[1] All individuals within health care environments in whom subclinical nasal carriage of *S aureus* and other potentially pathogenic bacteria is present contribute to the burden of infection risk to themselves and others. Nasal colonization is known to be predominantly localized in the anterior, vestibular region of the nasal anatomy.[2]

Data support the premise that individuals exhibiting subclinical nasal colonization by *S aureus* can be grouped into persistent, intermittent, and noncarrier types.[3-5] In a study using artificial inoculation, carriage characteristics were similar in intermittent carrier and noncarriers (comprising 76% of the total), but distinct from those of the persistent carrier group.[6] These findings are consistent with the concept that either most individuals are actually intermittent carriers or are noncarriers who exhibit carriage only under environmental pressure (eg, recurring exposure).[6] In either instance, the demonstrated ability of these 2 groups to sustain transient subclinical carriage for 4-14 days on average would put either of them in a position to increase risk for *S aureus* infection in themselves or others with whom they come in contact during that period.

Within the health care community, there are several categories of individuals who maintain a long-term presence within that

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environment who are not screened or treated for *S aureus* carriage, but who may contribute to its presence. These include longer-term patients as well as health care professionals (HCPs) and support staff who regularly come in contact with patients. In a study of 256 HCPs at a large urban tertiary care teaching hospital,[7] including paramedics, nurses, clerical workers, and physicians, *S aureus* was isolated from the anterior nares of 43.8% of those screened with 6.6% exhibiting methicillin-resistant *S aureus* (MRSA) carriage. The authors point to 3 potential consequences of this carriage: self-infection of these workers by their own strains, cross-transmission to patients, and introduction of the pathogen into their communities.[7] Furthermore, a study using whole-genome sequencing to investigate MRSA transmission within a neonatal intensive care unit provided evidence of the complexity of transmission that can occur in both directions involving patients and caregivers.[8]

Strategies to reduce colonization in patients preadmission have been shown to be very successful. These have primarily focused on regimens that include nasal treatment with the antibiotic mupirocin.[9-12] Recently, a multicenter study suggested the potential utility of universal antibiotic treatment of patients at admission without screening for specific carriage to be an effective approach to reduce intensive care unit MRSA infections.[13] Although effective, strategies that incorporate wide use of antibiotics lead to increased opportunities for the development of resistant bacteria. For this reason, nasal antibiotics are typically not used on a regular basis to reduce subclinical colonization in individuals within the health care environment in whom prophylactic treatment might be beneficial. These could include patients with immune deficiency or who are otherwise at higher-risk for infection and longer-term patients, as well as HCPs and other staff who work in the patient environment.

The development of effective and convenient nonantibiotic nasal preparations for daily use could provide appropriate additional methods for infection control, addressing the well-known hand-to-nose-to-hand cycle of inoculation and contamination involving the nasal bacterial repository.[14] A nonselective antiseptic agent, such as ethanol, would be expected to reduce colonization by all strains of bacteria, similar to a broad-spectrum antibiotic, but with both gram-positive and gram-negative bacteria being affected and without the risk of resistance being developed. In patients, daily application of such an agent could reduce the risk of self-inoculation and contamination of the hospital room environment. The regular use of a nasal antiseptic by HCPs could reduce their involvement in the process of bacterial transference, as well as contribute to their own preventive and protective hygiene in the work environment.

The goal of our study was to determine the magnitude and breadth of bacterial reduction by a nonantibiotic, alcohol-based nasal antiseptic applied during a typical workday in primary HCPs. Study subjects included nurses and surgical technicians directly participating in patient treatment and care on the day of testing. Data were collected on the treatment effects on both *S aureus* and total bacterial carriage in the nasal vestibule during a single day of application.

METHODS

Selection and enrollment of study subjects

Volunteers were recruited from the nursing and technical staff working in the main and ambulatory operating rooms and patient care floors of the Medical University of South Carolina Hospital. This randomized double-blind, placebo-controlled study was approved by the Medical University of South Carolina Institutional Review Board (Pro000018198). This study is registered on clinicaltrials.gov (Identifier: NCT01861457).

Eligible to participate were healthy HCPs between ages 18 and 70 years who were able and agreed to refrain from using all nasal spray preparations or washes from the time of their screening through their scheduled study day. Exclusionary criteria included symptoms of upper respiratory disease, including chronic rhinitis/sinusitis, seasonal allergies, upper respiratory infection during the previous 4 weeks; the use of antibiotics in the 2 weeks before or during the study; a known allergy to citrus oil; or being a cigarette smoker. Nonsmokers were defined as those individuals who had abstained from smoking for at least 1 year before the study.

After obtaining informed consent, eligible subjects were screened by nasal swab for vestibular carriage of *S aureus* as described below. Subjects who screened positive and who accepted enrollment in the study were scheduled for participation within 10 days to minimize loss of carriage status by the study date.

Study protocol

The study period consisted of a single 10-hour workday, during which nasal swab samples from the right and left nasal vestibules of each subject were obtained and pooled (Fig 1). The first combined sample from each subject was collected by the medical study staff at the start of the workday (hour 0), immediately followed by application of the randomly assigned placebo or test preparation with a saturated swab to both nasal vestibules. Application of the placebo preparation was used to control for the potential mechanical effects of the application process, itself. Reapplications of the placebo and treatment preparations were made at hours 4 and 8. At hour 10, the subjects returned to enable collection of the posttreatment nasal sample by the medical study staff.

Preparation and application of the test and control agents

A commercially available, nonprescription product, Nozin Nasal Sanitizer antiseptic (Global Life Technologies Corp, Chevy Chase, Md) was used as the test agent in our study. The safety-tested formulation is composed of 70% ethanol active combined with a mixture of natural oil emollients and the preservative benzalkonium chloride. Sterile phosphate-buffered saline with 0.017% peppermint oil as a masking agent was used as placebo treatment control.

Application of the antiseptic or placebo control preparation was made by saturating a sterile swab with 5 drops (~200 uL) of solution and rotating the swab around the inside of the vestibular surfaces of both nostrils.

Sample collection and analysis

Nasal samples from both screening and study sample collection were obtained using sterile BD ESwab Collection Kits (Becton, Dickenson & Co, Franklin Lakes, NJ). For screening, neat samples were inoculated onto BBL CHROMagar *Staph aureus* medium (Becton, Dickenson & Co) and incubated at 35°C for 24 hours; mauve colonies were identified as *S aureus* by Gram's stain, catalase, and latex agglutination testing. For evaluation of treatment samples, duplicate 75 μL aliquots of neat and 1:10 dilutions of each sample were inoculated onto plates of BBL CHROMagar *Staph aureus* medium and tryptic soy agar with 5% sheep blood to assess *S aureus* and total bacterial colony forming units (CFU) counts, respectively. At 24 hours of incubation at 35°C, CHROMagar plates were photographed and mauve colonies were counted and identified as *S aureus* as described above. At 48 hours of incubation at 35°C, tryptic soy agar plates were photographed for determination of total bacterial CFU. All data from subjects whose baseline inocula