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Major Article

Long-acting water-stable organosilane agent and its sustained effect on reducing microbial load in an intensive care unit

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Background: Contaminated hospital surfaces contribute significantly to the transmission of health care-associated infections. Although disinfectants reduce bioburden by up to 99%, bacterial growth can rebound within hours to precleaning levels. We tested the effectiveness of an innovative, long-acting water-stable organosilane (WSO) to achieve sustained decreases in bioburden on hard surfaces.

Methods: A 5-month prospective, randomized, double-blind controlled study was performed. Eighteen intensive care unit rooms were randomly divided into placebo or treatment groups. Hard surfaces in all rooms were cleaned using the same protocol, except the placebo surfaces were cleaned with an inert saline solution and the treatment surfaces were treated with the WSO. Binomial regression with repeated measures were used to assess mean reductions in total bioburden as measured by colony forming units.

Results: The placebo resulted in average reductions in total colony forming units of 35% to 40% (relative risk reduction [RRR], 0.65; $P < .01$) and the WSO group averaged reductions of colony forming units by 66% to 99% (RRR, 0.55; $P < .001$). Total *Staphylococcus aureus* increased among the placebo rooms 30% (RRR, 0.69; $P < .001$), whereas in treatment rooms there was a reduction of 50%-60% (RRR, 0.57; $P < .01$). Although both sets of rooms saw reductions in bioburden or colony forming units, application of the WSO resulted in larger reductions. There was also greater variability in reductions in the placebo arm.

Conclusion: This is the first randomized, double-blind controlled study of an innovative WSO on high-touch hard surfaces at risk for high bioburdens. Sustained reductions of bioburden with the monthly application of this unique WSO may be associated with significant reductions in the risk of health care-associated infections.

Health care-associated infections (HAI) are a leading cause of morbidity and mortality in the United States and abroad. Data from 2011 estimated there were 721,800 HAIs annually in US hospitals alone,[1] resulting in approximately 75,000 deaths.[2] Financial consequences can be severe, both in direct costs[3] and payer penalties, for hospitals that incur HAIs.[4] Despite countless advances in patient safety with an increased focus on HAIs, HAIs continue to be prevalent, in part due to environmental conditions.

Although it is well documented, it is underappreciated that contaminated surfaces play a significant role in transmission of pathogens,[5-10] some of which will live for hours and up to several months depending on the bacteria and the surfaces.[11] Even after cleaning, hospital surface environments can rapidly recontaminate. In 2012, Attaway et al[12] showed that although standard hospital-approved disinfectant will reduce the intrinsic bacterial burden by up to 99%, bacteria levels rebound to above targeted levels within 2.5-6.5 hours postcleaning. Similarly, bacterial recontamination just 24 hours after treatment with vaporized hydrogen peroxide has also been documented.[13] Efforts to prolong the duration of suppressed bacterial bioburden are a critical step in preventing the risk of HAI transmission through hospital surfaces.

This study is the first double-blind controlled evaluation of a sustained surface antimicrobial agent (Goldshield 75; AP Goldshield, Locust Valley, NY). The beneficial in vitro effect of this antimicrobial agent on gowns has previously been reported.[14] Furthermore, a recent observational study demonstrated the positive influence

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of the antimicrobial agent on reducing bioburden on hospital hard surfaces.[15] The current study was conducted to determine the efficacy of the antimicrobial agent at sustaining a reduction in bioburden postcleaning in comparison to placebo.

The product is an Environmental Protection Agency-approved antimicrobial organosilane with an electrochemical mode of action that provides sustained in vitro reductions in microbes, including but not limited to methicillin-resistant *Staphylococcus aureus*, vancomycin-resistant *enterococci* (VRE), gram-negative bacteria, and influenza viruses. It is a water-stable surfactant that covalently bonds to surfaces with octadecyldimethylammonium ions, forming long carbon chains that electrochemically draw bacteria to them. Because of this mechanical kill, it is expected that bacteria will not form resistance to this product. In this study, we report for the first time the sustained decreases in microbial load on hard surfaces with the antimicrobial agent compared with placebo.

METHODS

Study design

This was a prospective, randomized double-blind control study conducted in the medical intensive care unit (MICU) of Genesys Regional Medical Center, a 410-bed community teaching hospital. Before the launch, the study was approved by the Genesys Health System Institutional Review Board. After the hospital's standard cleaning process, the rooms were treated in 2 different fashions. Half of the MICU rooms (9 beds) were randomized for cleaning with a placebo or saline solution (placebo). The other half of the MICU rooms (9 beds), were randomized for cleaning with the antimicrobial agent (treatment). For blinding purposes, the placebo solution was created to smell and look like the antimicrobial agent so the environmental services (EVS) staff, lab technicians, and research staff were unable to distinguish the difference.

The study was conducted over a 5-month period (October 2015-March 2016). Baseline colony forming unit data on hard surfaces from all 18 rooms was collected in the first 7 days. High-frequency contact surfaces, including bedrails, patient call pad, patient tray table, and bedside table drawer handle in the MICU rooms were sampled for colony forming unit growth weekly. Application of placebo or the antimicrobial agent was performed every 30 days, independent of sampling of surfaces. Because isolation room cleaning methods and procedures differ from standard protocol, reapplication was performed after the isolation room cleaning even when the 30-day mark had not been reached. A total of 342 rooms were sampled: 161 placebo rooms and 166 treatment rooms. Binomial regression with repeated measures was used to examine mean reductions in total bioburden and for total *Staphylococcus* and *S aureus, Enterococcus faecalis*, and *Enterococcus faecium* microorganisms as measured by colony forming units.

Protocol

Starting on October 14, 2015, samples were collected from all 18 patient rooms for 7 consecutive days (baseline) by blinded company affiliated microbiologists. Samples were collected using Environmental Sampling Kit swabs in 10 mL buffer (Puritan, Guilford, ME). Total bioburden counts were enumerated using standard methods agar. Total *Staphylococcus* and *S aureus* were enumerated using mannitol salt agar plates. *E faecialis* and *E faecium* were enumerated using Spectra VRE plates (Remel, San Diego, CA). Sample sites included patient bed rails (both larger rails on 1 swab), patient call pad, top middle edge of the patient tray table, and the top-drawer handle of the bedside table. These sites were selected based on their frequency of use by patients, visitors, and health care workers.

As described in Table 1, following the week of baseline sampling, 3 high-touch applications were performed in all 18 rooms with the respective group assignment. The initial 3 high-touch applications were performed on 3 consecutive days by the staff. Follow-up applications were performed by the hospital's EVS department staff every 30 days or after an isolation discharge clean where bleach was used. Whereas colony forming unit samples were only collected from the aforementioned locations in each room, all high-touch surfaces in the rooms were treated with either the antimicrobial agent or placebo.

Company-affiliated microbiologists were blinded to which rooms were treated with the antimicrobial agent and which received the placebo. Rooms were assigned randomly by members of the hospital's research department. A list of which rooms were group A rooms and which were group B rooms was provided to the hospital's EVS management and the EVS staff assigned to the study unit to ensure the correct bottle was used on applications; EVS staff members were blinded to the assignment of group A or B to placebo or treatment.

Before EVS staff members performed high-touch applications, all shifts of EVS staff were given 3 days of inservices on the high-touch procedure and the study. The EVS staff assigned to the MICU received 1-on-1 training in a patient room. Within a given day, the same EVS staff member cleaned both placebo and treatment rooms ensuring consistency in application and cleaning between groups. The company's staff made sure that assigned EVS always had an updated list of rooms that needed applications, and checked in with them weekly. The company provided protocols and a poster that was hung in the EVS office to ensure all staff members were aware of the study.

Collection of data

After the initial 3 high-touch applications, samples were collected weekly from all 18 rooms unless microbiologists were asked not to go into a room by medical staff. Samples were transferred in a cooler to a microbiology lab in the area, where they were pro-

Table 1
Sampling and application protocols

	Nonisolation room	Isolation room
Frequency of environmental services cleaning	Daily	Daily
Cleaning solution used	Virex (Sealed Air, Charlotte, NC)	Bleach wipes
Initial colony forming unit sampling	7 consecutive days at launch	7 consecutive days at launch
Initial application of placebo (group A) or antimicrobial agent (group B)	3 consecutive days following initial colony forming unit sampling completion	3 consecutive days following initial colony forming unit sampling completion
Reapplication of placebo (group A) or antimicrobial agent (group B)	Every 30 d	Every 30 d and following every discharge clean where bleach was used
Colony forming unit resampling	Weekly	Weekly

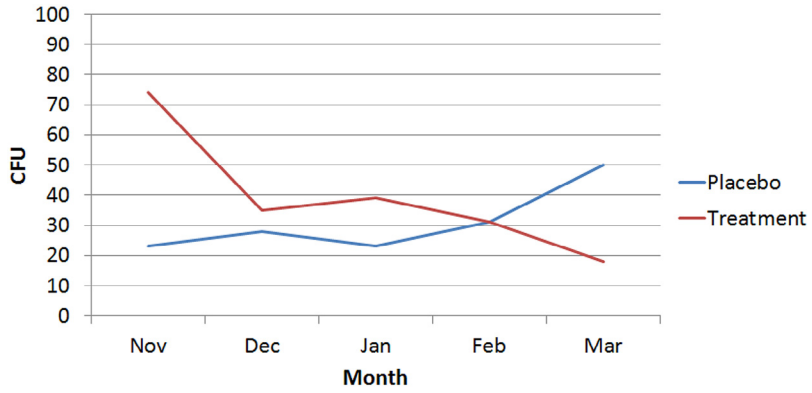

Fig 1. Average total bioburden colony forming unit count over time for bedrail sample site.

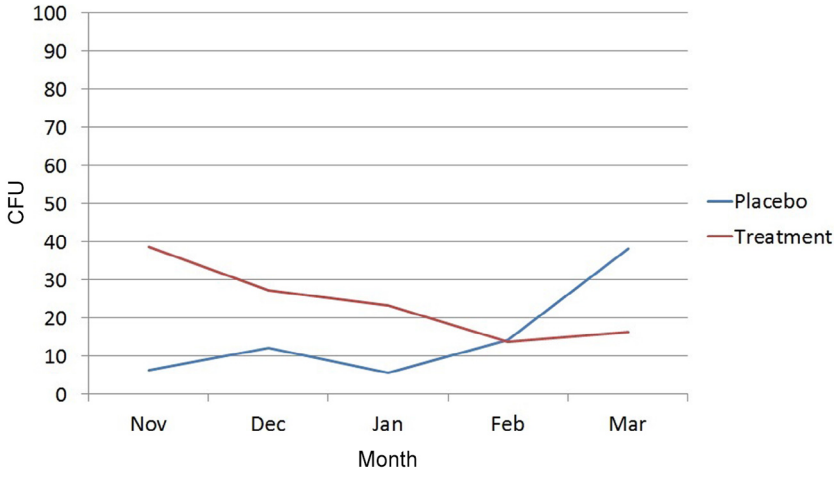

Fig 2. Average total *Staphylococcus* colony forming unit count over time for bedrail sample site.

cessed using spread plating. Samples were plated on standard methods agar (total bioburden), mannitol salt agar (total *Staphylococcus* and *S aureus*), and Spectra VRE agar (*E faecium* and *E faecalis*). Direct and 1:10 dilutions were plated and counted after 48 hours of incubation at 35°C±2°C.

Weekly bioburden measurements were obtained and averaged for the month. The average bioburden for each type of microbial load was compared monthly over a 5-month time frame. Utilizing a 2-group repeated measures analysis of variance, average burden by treatment was tested for significant change over time at $P < .05$. Assumption of sphericity was tested by Mauchly's statistical test. Descriptive statistics on group and subgroup burden was conducted with means±standard deviation and frequency counts (n [%]). A power calculation to determine an effect size of 20% or greater difference between groups at each time point required a minimum of 575 in each group would yield 80% power to detect the differences as significant at $P < .05$.

Although reductions in VRE *(E faecium* and *E faecalis)* were also observed, bacteria counts were too low to observe trends.

RESULTS

There were 342 rooms sampled over the 5-month study period with 161 rooms randomly assigned to placebo and 166 rooms assigned to treatment. In total, 1,382 samples were collected (680 samples from placebo rooms and 702 samples from treatment rooms). There were no differences in room designations between the treatment and placebo groups for occupied (78.9% vs 78.3%; $P = .89$), isolation (15.1% vs 12.4%; $P = .48$), and clean (6.0% vs 9.3%; $P = .26$). Bedrail bioburden at baseline did differ between the groups. Treatment rooms had higher total bioburden and higher *Staphylococcus* levels than placebo rooms at the beginning of the study (Fig 1). A significant reduction in total bioburden and *Staphylococcus* were observed following study completion with a more dramatic reduction demonstrated by the treatment group rooms. The reduction in total bioburden from baseline was 35.1% for placebo and 65.9% treatment. For both groups, a significant reduction was achieved ($P \leq .01$ placebo and $P \leq .001$ treatment). A significant reduction was also achieved between the placebo and treatment groups ($P = .02$) (Fig 1).

The reduction for treatment rooms was significantly greater than for placebo (absolute difference, 30.8% and relative difference, 46.7%; $P = .2$). Reduction in total *Staphylococcus* was 40.7% for placebo and 76.3% treatment. A significant reduction was achieved between the treatment and placebo groups for total *Staphylococcus* ($P = .02$) (Fig 2).

Over the 5-month period, total bioburden was reduced within a range of 35%-90% for both groups and all surfaces, depending on site of application.

DISCUSSION

Although the role of hard surfaces in HAI transmission has been well documented,[5-10] there is a paucity of data identifying the optimal method to sustain a reduced bioburden.[13,14] Our work describes a

statistically significant sustained reduction in bacterial bioburden for the antimicrobial agent over placebo as measured by colony forming unit counts.

This trial confirms in a double-blind fashion what other studies have observed. The antimicrobial agent produces sustained reductions in the overall bacterial bioburden.

The prevention of HAIs takes a multidisciplinary approach. One of the ways hospitals can achieve this is through the standardization of cleaning methods. Our findings suggest that along with following evidence-based standards for room cleaning, sterilization,[16] and hand hygiene,[17] the antimicrobial agent creates a sustained reduction in environmental bacterial bioburden to further reduce the risk of HAIs.

A limitation of this study was that of bed movement. Randomization occurred at the level of the room with some beds moving from room to room after the study was initiated. We tracked bed movement during the study and observed that <10% of beds changed rooms and this level of movement is not large enough to influence the significance of the findings.

Another limitation of this study is that it did not study the direct relationship between the product and incidence of HAI. There is an underlying assumption that environmental contaminants will increase HAIs, and because this study looked at bacterial bioburden on hard surfaces it does not speak directly to reduction in HAIs.

Strengths of this study include the large number of rooms evaluated, the randomized, double-blind design, and the multidisciplinary team that was used to incorporate this product. We did note a difference in bioburden at the initial measurement phase. However, the rooms were allocated by a computerized, randomly generated assignment. The higher surface burden among the treatment rooms at the initial measurement was likely due to chance. Despite this difference initially, the overall results remain the same, with the treatment rooms showing an overall greater decrease in bacterial bioburden than control rooms.

CONCLUSIONS

As with all practices in infection prevention, environmental stewardship requires a multifaceted approach to reduce the risk of HAIs. Sustaining a reduced bioburden on hospital hard surfaces should be the pinnacle objective of this practice. This study shows that application of a long-acting water-stable organosilane antimicrobial agent in addition to improved standard cleaning procedures reduces overall bacterial burden as well as total *Staphylococcus* when compared with placebo. Although these results are promising, further research is required to determine the direct implications on HAI rates relative to sustained reductions in bioburden.

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