Suppression of regrowth of normal skin flora under chlorhexidine gluconate dressings applied to chlorhexidine gluconate-prepped skin

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Intravascular (IV) catheters are widely used in patient care for administration of fluids, medications, blood products, and parenteral nutrition, as well as for insertion of pacing electrodes and hemodynamic measurements. There are over 150 million IV devices placed in the United States each year. Whereas the majority of these devices are peripheral IV catheters, over 5 million are central venous catheters.

Catheter-related bloodstream infections (CRBSIs) resulting from use of intravenous catheters are a serious medical problem associated with significant morbidity and mortality and are the fourth most common type of hospital-acquired infection. Over 90,000 infections occur per year in hospitals in the United States, and up to 25% of these cases are fatal. Despite decreases in CRBSI rates, ranging from 38% to 54%, reported by intensive care units across the United States, recent data from the Centers for Disease Control and Prevention’s (CDC’s) National Healthcare Surveillance Network indicate that the current incidence is approximately 3 infections per 1,000 catheter-days. In addition to serious health consequences, CRBSIs have a significant economic impact. On average, a patient with a CRBSI can spend an additional 9.6 to 14.3 days in the intensive care unit. The attributable cost for this type of infection is estimated to be between $0.59 and $2.68 billion dollars annually.

Catheters provide an access point for bacteria to enter the body, leaving patients at risk for local and systemic infections. Catheter colonization and potential bloodstream infection during the first week after insertion of a central venous catheter have been shown to result from the patient’s skin flora. In fact, skin flora at the insertion site have been shown to be the most common source of catheter colonization. Although the use of chlorhexidine gluconate (CHG) with isopropyl alcohol (IPA) for antisepsis of the skin prior to catheter insertion provides substantial protection, viable bacteria may still remain on the skin, and regrowth occurs over time. Using an antimicrobial dressing to seal and secure the catheter may reduce the incidence of catheter colonization and subsequent infections, hence the need for the study that was undertaken.

The primary objective of the study was to compare a nonantimicrobial polyurethane film dressing to 2 CHG-containing dressings applied to chlorhexidine gluconate-prepped skin.

**Key Words:** Antimicrobial, Catheter, CHG, Chlorhexidine, Catheter-related bloodstream infections, CRBSI, Dressing

**Background:** Catheter colonization and bloodstream infection during the first week after insertion of a central venous catheter have been shown to result from the patient’s own skin flora.

**Methods:** The backs of 32 healthy subjects were prepped with a 2% chlorhexidine gluconate (CHG)/70% isopropyl alcohol antiseptic. Three dressings, 2 of which contained CHG, were placed on the prepped skin in a randomized design. Samples of aerobic bacteria were collected using the cup scrub method. Skin under the dressings was sampled by quadrant on days 1, 4, and 7. Relative suppression of regrowth was compared using an adjusted paired t test.

**Results:** Mean log counts were 3.2 log10 colony-forming units (CFU)/cm² before antisepsis and 0.4 after antisepsis. Mean log counts obtained on days 1, 4, and 7 were 0.4, 0.3, and 0.5 log10 CFU/cm² for the CHG gel; 0.4, 0.4, and 0.9 log10 CFU/cm² for the CHG disk; and 0.9, 1.2, and 1.5 log10 CFU/cm² for the Control, respectively.

**Conclusion:** Skin flora was not completely eradicated during antisepsis, and bacterial regrowth occurred postantisepsis. The use of CHG dressings helped sustain a reduced bacterial count on the skin. The continuously releasing CHG gel maintained suppression to a greater extent than the CHG disk at 7 days (P = .01).
insertion site dressings with respect to the abilities of the CHG-containing dressings to suppress bacterial regrowth over a 7-day time frame in healthy adults. The secondary objective was to compare the relative performance of each of the CHG-containing dressings against each other.

MATERIALS AND METHODS

Test materials

Three commercially available central catheter dressings were evaluated. The “Control” was 3M Tegaderm Transparent Film Dressing (3M Health Care, St. Paul, MN), a polyurethane film without CHG. The “CHG gel” was 3M Tegaderm CHG IV Securement Dressing (3M Health Care), a catheter securement device with a continuously releasing hydrogel containing 2% CHG by weight. The “CHG disk” was the 1-inch diameter with 4-mm center hole BIOPATCH Protective Disk with CHG (Ethicon, Inc, New Brunswick, NJ), a dry CHG-containing disk.

Study population

A total of 32 healthy male and female volunteers, 18 years of age or older, with no dermatological conditions or known history of sensitivity to acrylates, natural rubber latex, CHG, or alcohol was enrolled into the study. Subjects with a history of diabetes, those undergoing antibiotic treatment, and pregnant or nursing women were excluded. The study was performed at a research facility with its own institutional review board, which approved the protocol, and all subjects provided written consent prior to participation.

Screening phase

All study participants underwent a 2-week washout period, during which they agreed not to use any antimicrobial products, harsh household chemicals, chemically treated recreational water systems, such as swimming pools and hot tubs, or ultraviolet tanning beds. Subjects were supplied with a nonantimicrobial personal hygiene kit for exclusive use during the screening and treatment phases of the study. They were instructed to refrain from bathing or showering during the 72-hour period prior to any baseline sample collection. If necessary, hair in the test areas was clipped not less than 48 hours before sampling.

At the end of the 2-week period, subjects were prescreened to evaluate the levels of normal flora on their backs. All aerobic microbial sampling for this study was performed using the Williamson-Kligman scrub cup technique and a sampling solution containing appropriate neutralizers. The scrub cup technique is the method specified for skin flora testing by the Food and Drug Administration and is described, along with the composition of the sampling solution, in the Bacterial Enumeration Methods section below. The sampling solution was evaluated prior to starting the study to ensure that the CHG was effectively neutralized and that there were no toxic effects on the growth of microorganisms. Subjects were allowed to continue into the treatment phase of the study if their average baseline counts were greater than or equal to 2.5-log10 colony-forming units per square centimeter (CFU/cm²).

Treatment phase

The 7-day length of the study was based on the CDC Guidelines for the Prevention of Intravascular Catheter-Related Infections, which recommends changing transparent dressings at least every 7 days. Subjects were not allowed to shower during the treatment phase; however, sponge-bathing (excluding the back) was permitted.

At the beginning of the treatment phase, 4 baseline samples of normal flora were collected from each subject: 2 at the center upper back and 2 at the center lower back (see Fig 1). Each subject’s back was divided into 4 quadrants: 2 on the upper back and 2 on the lower back. Each quadrant contained 4 treatment sites (post-antisepsis, CHG gel, CHG disk, and Control) and was assigned to 1 sampling day (day 1, day 4, day 7 primary, or day 7 secondary). The placement of treatments within each quadrant and the sampling day were assigned according to a computer-generated randomization schedule. In case of compromised dressing integrity in the primary quadrant for day 7, a secondary quadrant was used. Subjects were replaced if the CHG gel or Control dressings were compromised on any of the sampling days.

Antisepsis was carried out using a commercially available skin preparation containing 2% CHG in 70% IPA (ChloraPrep Antiseptic Skin Prep; CareFusion Corporation, San Diego, CA), which was applied to the subject’s back using light friction and a back and forth motion for 30 seconds, according to the manufacturer’s instructions for dry sites. Postantisepsis sampling was performed once the skin was visibly dry, at least 30 seconds after completion of prepping.

Following collection of the postantisepsis samples, the test materials were applied by quadrant according to the randomization schedule. The CHG disk dressing, which requires the use of an additional adhesive dressing to keep it in place, was covered with a nonantimicrobial transparent film dressing. To aid in maintaining dressing integrity, a half-inch wide film of Mastisol Liquid Adhesive (Ferndale Laboratories, Inc, Ferndale, MI) was applied along the outer edges of all test sites and allowed to air-dry for 30 seconds prior to application of the dressings. Subjects were instructed to continue to avoid the use of antimicrobial products, harsh chemicals, chemically treated recreational water systems, and ultraviolet tanning beds. They were also instructed to avoid prolonged moisture contact with the samples and vigorous activities that may cause sweating.

Dressings were removed 1 test quadrant at a time on days 1, 4, and 7, and the skin beneath each dressing was sampled.
Suppression of regrowth was determined by comparing the microbial counts in the samples collected under the dressings on days 1, 4, and 7 against the corresponding postantisepsis counts. The skin underneath each test material was also evaluated for irritation based on a rating scale from 0 to 3 with 0 indicating no erythema, edema, or vesiculation and 3 indicating a severe reaction. Skin irritation and dressing integrity were monitored on days 2, 3, 5, and 6. If necessary, the outer edges of the dressings were reinforced by taping.

Bacterial enumeration methods

Quantitative cultures were obtained using the scrub cup technique. To guarantee that only the skin in contact with CHG was sampled, the scrub cup was a smaller size than the dressings and the sampling area was at the center of the application site of each dressing. The sampling solution used contained 75 mmol/L phosphate buffer and 0.1% t-octylphenoxypolyethoxyethanol, along with 3.0% polysorbate 80 and 0.3% lecithin for neutralization of the CHG. A 2.5-mL aliquot of sampling solution was pipetted into the sampling cylinder, and the skin was scrubbed with moderate pressure for 1 minute using a sterile rubber policeman. An additional 2.5 mL of fresh sampling solution was added to the cylinder, and the scrubbing procedure was repeated. This solution was pooled with the first sample.

Ten-fold serial dilutions of the samples were then performed using Butterfield’s phosphate-buffered water. Samples were poured plated in duplicate using trypticase soy agar containing neutralizers. The resulting plates were incubated aerobically for 72 hours at 30°C ± 2°C and enumerated by standard plate-counting procedures.

Raw data (colony-forming units/millilitre) was converted to log_{10} CFU/cm². Counts of less than 1 CFU/cm² were treated as 1 CFU/cm², such that the log transformation was zero. Log regrowth was calculated for each test site by subtracting the log values at postantisepsis from the day 1, day 4, or day 7 log values.

Evaluation of neutralization efficacy and toxicity

Two subjects were enrolled to perform an in vivo neutralization validation on the sampling solution containing neutralizers. The skin on their backs was prepped with ChloraPrep for 30 seconds and allowed to air-dry for at least 30 seconds. After drying, post-prep samples were collected using the scrub cup technique and evaluated for neutralization (see below) prior to application of the test dressings. Duplicate samples of all 3 dressing types were applied and worn for 1 day and 7 days by each subject. At each time point, samples were collected using the scrub cup technique and inoculated with low levels of a marker organism, tetracycline-resistant *Staphylococcus aureus*, ATCC 27217. Two contact times, immediately (<1 minute) and 30 minutes, after inoculation were evaluated to confirm efficacy of the neutralizer during the time between sample collection and plating. Toxicity of the sampling solution containing neutralizers was also evaluated immediately and at 30 minutes postinoculation.

Statistical analysis

This study was a randomized blocked design where each subject received each treatment. Assuming a 1.5 log standard deviation, with 2-sided α = 0.05 and 80% power, 30 completing subjects were required to detect a 0.8 log difference in bacterial regrowth.

The log regrowth value at each day (1, 4, and 7) was compared between treatment groups using a paired t test. The Holm Stepwise test was used to adjust for multiple comparisons involving the paired difference in log counts between CHG gel and Control, CHG disk and Control, and CHG gel and CHG disk at days 1, 4, and 7. A separate analysis was performed on each day using all the data available for that day. Significance was assessed at $P < .05$ (2-tailed).

RESULTS

Demographic and baseline characteristics

A total of 72 subjects were screened, of which 32 met the screening baseline count requirements and were enrolled into the study. Of the subjects who were not enrolled, 38 had low microbial counts, 1 had sutures on their back, and 1 qualified but was not needed for enrollment.

A total of 30 subjects completed the study. Although dressings were applied to the 32 subjects who met the screening baseline count requirements, only 31 of these subjects were evaluable. One subject failed to meet the baseline count requirements at the start of the treatment phase, and these data were not included in the analysis. Of the 31 evaluable subjects, 1 had lost all dressings by day 4 and was replaced by a subject who assumed the same randomization. The baseline, postprep, and day 1 data for the replaced subject were included in the analysis. One subject lost the day 7 CHG disk samples and was not replaced.

The mean (standard deviation [SD]) screening baseline count was 3.29 (0.497) log_{10} CFU/cm² with a minimum and maximum of 2.5 and 4.4 log_{10} CFU/cm², respectively. The mean (SD) treatment day baseline count was 3.12 (0.524) log_{10} CFU/cm², with a minimum and maximum of 1.5 and 4.3 log_{10} CFU/cm², respectively. The majority (72%) of the subjects was male. The mean (SD) age was 41 (16.5) years. The predominant races were white (53%), African American (22%), and Asian (19%).

Treatment day baseline and postprep counts

After antisepsis, the log counts decreased to a mean of 0.35 log_{10} CFU/cm² with values ranging from 0.12 log_{10} CFU/cm² (limit of detection) to 0.98 log_{10} CFU/cm² (Table 1). Forty-five percent (14/31) of the evaluable subjects had mean postantisepsis counts of 0.12 log_{10} CFU/cm²; 23% (7/31) had between >0.12 and 0.5 log_{10} CFU/cm²; and 32% (10/31) had between >0.5 and 1.0 log_{10} CFU/cm². One subject did not meet the treatment day baseline criterion and was therefore excluded from the efficacy analysis.

Log regrowth

Log regrowth was defined as the increase in log count on any given day relative to the day 0 postantisepsis log count. The mean log regrowths obtained from the CHG gel sample sites were 0.02, 0.01, and 0.002 log_{10} CFU/cm² on days 1, 4, and 7, respectively, and the mean log regrowths obtained from the CHG disk sample sites were 0.01, 0.07, and 0.45 log_{10} CFU/cm² on days 1, 4, and 7, respectively. The Control sample sites showed mean log regrowths of 0.57, 0.85, and 1.0 log_{10} CFU/cm² on days 1, 4, and 7, respectively. Results are summarized in Table 1. The distribution of the log regrowth values is shown in Figure 2.

Log counts at days 1, 4, and 7

The mean log counts obtained from the CHG gel sample sites were 0.40, 0.34, and 0.45 log_{10} CFU/cm² on days 1, 4, and 7, respectively; and the mean log counts obtained from the CHG disk sample sites were 0.39, 0.40, and 0.91 log_{10} CFU/cm² on days 1, 4, and 7, respectively. The Control sample sites showed mean log
The mean values of the paired difference between CHG gel and the Control samples were $0.01, 0.06,$ and $0.45 \log_{10} \text{CFU/cm}^2$ on days 1, 4, and 7, respectively (see Fig 3).

**Paired comparisons**

The mean values of the paired difference between CHG gel and the Control samples were $0.01, 0.06,$ and $0.45 \log_{10} \text{CFU/cm}^2$ on days 1, 4, and 7, respectively. The adjusted paired t test yielded significant $P$ values at all 3 time points ($P < .001$), providing evidence that the mean log count under the CHG gel dressing was significantly lower than that under the Control dressings from day 1 to day 7.

The mean values of the paired difference between CHG disk and the Control samples were $0.45, 0.79,$ and $0.62 \log_{10} \text{CFU/cm}^2$ on days 1, 4, and 7, respectively. The adjusted paired t test yielded significant $P$ values at all 3 time points ($P < .001$ on days 1 and 4, and $P = .01$ on day 7), providing evidence that the mean log count under the CHG disk dressing was significantly lower than that under the Control dressings from day 1 to day 7.

The mean values of the paired difference between CHG gel and the CHG disk samples were $0.01, -0.06,$ and $-0.45 \log_{10} \text{CFU/cm}^2$ on days 1, 4, and 7, respectively. The adjusted paired t test yielded a significant $P$ value on day 7 ($P = .01$), illustrating that the mean log count under the CHG gel dressings was significantly lower than that under the CHG disk dressings at that time point.

**Safety evaluation**

No adverse events were recorded during the study. In addition, no incidence of erythema, edema, or vesiculation was reported at any test site, indicating that the CHG gel, CHG disk, and Control were well tolerated by the study population.

**DISCUSSION**

One approach to decreasing CRBSI rates has been the implementation of bundled interventions. The prevention bundle generally includes an educational program for health care workers, appropriate hand hygiene, use of chlorhexidine skin antisepsis, use of maximal barrier precautions for catheter insertion, avoidance of
the femoral vein, prompt removal of unnecessary catheters, and monitoring of the insertion site. Implementation of these bundles has markedly reduced the rates of CRBSIs at many facilities. However, the current incidence rate remains at approximately 3 infections per 1,000 catheter-days.

Additional measures designed to further reduce CRBSIs include the use of antimicrobial-impregnated devices, such as catheters and dressings. A meta-analysis of several small or unpublished studies has suggested that placement of a CHG-impregnated dressing over the catheter insertion site results in a significant decrease in vascular and epidural catheter colonization and a nonsignificant decrease in catheter-related bloodstream infections. Recently, a large, multicenter, randomized controlled trial was conducted showing that the use of a dressing incorporating a CHG disk decreased the rates of CRBSI from 1.3 per 1,000 catheter-days to 0.4 per 1,000 catheter-days.

These studies indicate the potential value that can be achieved through the use of CHG-impregnated dressings. To this end, the current study evaluated the abilities of the CHG disk and a newly introduced catheter securement dressing that integrates a CHG gel pad with a transparent breathable dressing for their abilities to suppress regrowth of normal skin flora when used after CHG-based antisepsis.

In 2 previous studies on healthy volunteers, the performance of the CHG disk and the CHG gel were compared. The first study showed the CHG gel to be significantly more effective than the CHG disk in reducing microbial counts on unprepped skin over a 10-day period (P < .008). The second study demonstrated the ability of CHG gel and CHG disk dressings to maintain bacterial log counts lower than the average postantisepsis count for up to 10 days on subclavian sites prepped with 70% IPA. The second study also showed that CHG gel was significantly more effective than CHG disk (P < .02) at preventing regrowth of skin flora on day 7, although on day 10 no significant difference was found. The study described in this paper corroborates the results from these previous studies and provides evidence of the effectiveness of CHG-impregnated dressings on skin prep with a CHG-containing skin antiseptic.

This study enrolled healthy subjects, utilized the back as the test site, and did not include broken skin or catheters. Potential limitations related to the lack of catheter use result from sampling under the CHG disk, which may include a region where no CHG is present, and from sampling under the CHG gel, which included no region where CHG was absent. However, additional data indicate that the CHG in the CHG gel migrates to the skin underlying the catheter, and, as a result, the availability of CHG in this situation is representative of its performance clinically.

The results from this study show that both of the CHG-containing dressings maintain significantly lower counts than the Control on skin prep with a CHG-containing skin antiseptic for all days sampled (P < .001). Compared with a mean postantisepsis level of 0.35 log_{10} CFU/cm², CHG gel and CHG disk suppressed regrowth of normal skin flora for up to 7 days, maintaining counts below 0.5 and 1.0 log_{10} CFU/cm², respectively. The current study also showed that the CHG gel suppressed bacterial regrowth at 7 days in a manner superior to the CHG disk (P < .01).

CONCLUSION

The results of this study demonstrate that low levels of skin flora remain viable after antisepsis with a CHG-containing skin prep and that regrowth of these organisms does occur over time. However, the use of dressings containing CHG will help maintain the low counts observed postantisepsis. In particular, the use of CHG gel maintained postantisepsis bacterial levels for 7 days and showed significantly lower counts than CHG disk (P = .01) at the 7-day time point. Because there are no data clearly demonstrating the threshold number of organisms above which CRBSIs occur, maintaining the lowest possible number of skin organisms may prove advantageous in preventing these infections.

References

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