A Novel Integrated Chlorhexidine-impregnated Transparent Dressing for Prevention of Vascular Catheter-related Bloodstream Infection: A Prospective Comparative Study In Healthy Volunteers

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ABSTRACT

Background: Most catheter-related bloodstream infections caused by short-term noncuffed central venous and arterial catheters derive from cutaneous microorganisms colonizing the insertion site. Technologic innovations to continuously suppress the cutaneous microflora about the catheter can materially reduce the risk of catheter-related BSI.

Objective: To better understand potential efficacy for prevention of catheter-related bloodstream infection with noncuffed vascular catheters and subjects’ tolerance of two chlorhexidine gluconate (CHG)-impregnated catheter site dressings, a CHG-impregnated sponge dressing (Biopatch™, Johnson and Johnson), designed to be affixed about the catheter, then immobilized with a nonmedicated polyurethane dressing, and a novel integrated CHG-impregnated transparent polyurethane dressing (Tegaderm™ CHG, 3M).

Design: Measurement of immediate surface antimicrobial activity (quantitative kill over 15 minutes) of the new integrated CHG dressing and a nonmedicated polyurethane dressing (control) against 15 clinical isolates representing 9 species, and two open-label in vivo trials in healthy volunteers of immediate and long term cutaneous antimicrobial activity, one analyzing prevention of skin flora regrowth on alcohol prepped subclavian sites and the other, cumulative kill of skin flora on unprepped sites over 10 days of exposure.

Setting: Medical Division Laboratories of 3M Company and Hill Top Research, Inc., Miamiville, OH.

Participants: Forty-eight healthy adults without primary skin disease or known allergy to CHG participated in the regrowth study on prepped subclavian sites and 29 subjects participated in the trial assessing kill of normal flora on unprepped skin.

Results: The new integrated CHG transparent dressing provided excellent in vitro kill when microorganisms were applied to the CHG surface of the dressing. In the regrowth trial, at day 7, the new integrated CHG transparent dressing showed significantly lower regrowth post prep compared to the control (P<0.0001). At day 10, both CHG dressings showed significantly lower regrowth (P<0.0003). There was a statistically significant difference between the new integrated CHG-impregnated transparent dressing and the CHG-impregnated sponge dressing at day 7 (∆ log₁₀ CFU 0.80, P≤0.02). In the unprepped study, the new dressing showed significantly higher log reductions at day 1 and day 4 (day 1 ∆ log₁₀ CFU/cm² 0.60 and day 4 ∆ 0.80) (P≤0.03; P≤0.0008). All three dressings were well tolerated, with none producing hypersensitivity.

Conclusions: Both CHG dressings provided excellent long-term surface antimicrobial activity against diverse microbial species and cutaneous floral suppression, and were well tolerated. The new integrated transparent CHG-impregnated dressing provided superior prevention of floral regrowth on prepped sites and progressive kill of the cutaneous microflora on unprepped sites. The new integrated transparent CHG-impregnated dressing is easier to apply, reliably secures the catheter, permits continuous inspection of the insertion site, obviates the need for every-other-day site care and warrants evaluation in a prospective randomized clinical trial.

INTRODUCTION

Short-term non-cuffed and non-tunneled central venous and arterial catheters are widely used inpatient care. The most frequent life-threatening complication of vascular access is catheter-related bloodstream infection (CRBSI), which is associated with significant morbidity, prolongation of hospitalization, excess healthcare costs and transfusional mortality.1-3 Most CRBSIs with short-term catheters are caused by cutaneous microorganisms from the insertion site.3-5 The use of chlorhexidine gluconate (CHG) for cutaneous antisepsis prior to catheter insertion provides substantial protection against CRBSI,3,6 however, the microflora can rapidly grow back and invade the catheter tract and cause infection.3,6

A novel CHG-impregnated hydrophilic vascular access site dressing has been developed which can be affixed to the skin about a percutaneous catheter at the time it is inserted (Biopatch™, Johnson and Johnson, Dallas, TX); the dressing maintains a high concentration of CHG on the underlying skin surface,11 and clinical trials have shown the dressing provides significant protection against colonization of catheters and CRBSI.6,10

A new integrated transparent CHG-impregnated vascular access site dressing has been developed (Tegaderm™ CHG, 3M, St Paul, MN) which is easier to apply, reliably secures the catheter and permits continuous inspection of the insertion site. We report comparative analyses of the two novel CHG-impregnated dressings in healthy volunteers to measure relative bactericidal surface activity at the site for prevention of CRBSI and subjects’ tolerance of the dressings.

References
Features of the two CHG-impregnated Dressings
The established CHG dressing studied (Biopatch™) is a hydrophilic polyurethane semipermeable absorptive foam disc 1 inch in diameter with a central hole and radial slit (Figure 1), impregnated with 86.5 mcg of chlorhexidine gluconate per mg dry weight. The dressing is conformable, highly permeable to water vapor, and can absorb up to eight times its weight in fluid; chlorhexidine incorporated into the dressing is released onto the skin surface beneath the dressing at a controlled rate for at least 7 days.11 The dressing is designed to be affixed to the skin surface around a percutaneous vascular catheter, then immobilized and covered with a sterile nonmedicated polyurethane dressing, to inhibit microbial growth on the site and prevent invasive infection of the catheter tract.

The gel rapidly softens at skin temperatures and flows about the catheter, providing intimate contact of the CHG-impregnated surface with the entire insertion site (Figure 2). The gel also absorbs up to eight times its weight in fluid, preventing accumulation of moisture on the site. The integrated dressing tightly secures the catheter, preventing any pistoning movement that can facilitate entry of microorganisms into the insertion tract.1

FIGURE 1. The chlorhexidine-impregnated sponge dressing.

FIGURE 2. The novel integrated CHG-impregnated transparent dressing.

METHODS

In Vitro Time-kill Study
The bactericidal surface activity of the new integrated CHG-impregnated transparent dressing was tested against a panel of 15 microbial strains obtained from the ATCC collection: methicillin-sensitive Staphylococcus aureus (2 strains), methicillin-resistant S. aureus (MRSA) (2 strains), Micrococcus luteus, Enterococcus faecalis (2 strains), vancomycin-resistant Enterococcus faecium, Escherichia coli (2 strains), Serratia marcescens, Pseudomonas aeruginosa (2 strains), and Candida albicans.

The established CHG-impregnated transparent dressing was each inoculated with 50-µL of a suspension containing 5 x 10^3 CFU/mL ±0.5 log. Inoculated dressings were covered and incubated at 35 ±2 °C then sampled in duplicate at 1, 3, 5, 10 and 15 minutes by immersing the entire dressing into 20 mL of PBS containing 0.04% KH2PO4, 1.0% Na2HPO4, 0.1% Triton X100 and the neutralizers, 0.9% lecithin, and 6.0% Tween 80 (pH 7.9), then vortexing for 2 minutes. The capacity of the neutralizers to immediately quench any carry-over CHG activity in the sampling solution was validated. Immediately after vortexing, ten-fold serial dilutions in phosphate-buffered water were plated in duplicate onto TSA (Difco, Detroit, MI) and plating within 20 minutes. The lower limit of detection for the culture method was 20 CFU/mL. After incubating overnight at 35 ±2 °C, counts on duplicate plates were averaged and converted to log10 CFU/mL, permitting measurement of a time kill curve.

Source of Subjects for In Vivo Trials
These studies were approved by an external IRB. Healthy adult volunteers not known to be allergic to CHG and without a primary skin disorder were informed of the nature of the study before written consent to participate was requested. Subjects were screened for high baseline cutaneous bacterial counts (skin floral densities ≤2.5 log10 CFU/cm²).

Subjects agreed not to participate in other studies and to refrain from using any systemic antimicrobials or cutaneous antiseptics 14 days prior to and during the study.

The Regrowth Study was conducted at HillTop Research in Miami, OH. Forty-eight subjects were enrolled, and 32 completed the study. Average age of subjects was 52 years (range 25-70), 51% were female and most (88%) were non-hispanic Caucasian; 12% were African-American. Average height was 67 inches, average weight 162 pounds, mean BMI 24.9.

The Unprepped Study was conducted in the Medical Division Laboratory of 3M Company in St Paul, MN. A total of 29 subjects were enrolled. Twenty subjects completed the 4 time points and 10 subjects completed all 5 time points.

The average age of subjects was 47 years (range 27-62), 55% were female and 97% non-hispanic Caucasian. The average height of the was 67 inches and average weight 183 pounds; the mean BMI was 28.3.


served as his or her own control by using five test sites over each
was a within-subjects randomized design in which each subject
cutaneous prepping for 1 minute with 70% isopropyl alcohol. This
Study of Suppression of Regrowth on Prepped Subclavian Sites
dressing (Tegaderm™ and Biopatch™ cutaneous antimicrobial activity of the two CHG (Tegaderm™
healthy volunteers to assess the immediate and long term surface
Two open-label
In Vivo
Trials in Volunteers
Two open-label in vivo comparative trials were conducted in
Microbiological Methods for In Vivo Trials
The same microbiological sampling method was used in both of
quantitative cultures were obtained using the Williamson-Kligman scrub cup technique, designated by
A sterile scrub cup (2.54 cm) is placed on the sampling site and
In Vivo Time Kill of Normal Flora on Unprepped Skin:
On study-day 0, two randomized skin sites on each of the two test
areas (one on the right and the other on the left) were sampled for
quantitative skin cultures were obtained, using the PBS sampling
solution containing neutralizers.
In Vivo Trials in Volunteers
Two open-label in vivo comparative trials were conducted in
Study of Suppression of Regrowth on Prepped Subclavian Sites
This study was conducted in the volunteers to assess the capaci
cutaneous prepping for 1 minute with 70% isopropyl alcohol. This was a within-subjects randomized design in which each subject
as served as his or her own control by using five test sites over each
subclavian vein (Figure 3).
were replaced with the value from the previous non-missing day, the
reduction from baseline was used to compare the effects of treat
On study-day 0, two skin sites located in the center of the two
subclavian test areas were sampled for baseline floral counts.
was prepped with 70% isopropyl alcohol for 1 minute. After the site air
dried, an immediate post-prep skin flora sample was obtained and
the three test dressings were applied following a randomization
schedule; the CHG-impregnated sponge dressing was immo-
and covered with a nonmedicated transparent dressing
(Tegaderm™, 3M). The dressings were left in place for 7 or 10
days. Quantitative skin cultures by the scrub cup technique were obtained from one side (by random assignment) after 7 days and
the contralateral side after 10 days.
RESULTS

In Vitro Time-kill Study
The study showed minimal log$_{10}$ reductions (<0.28 log) of any of the test strains on the nonmedicated control dressing, whereas log$_{10}$ reductions ranged from 3.22 to 6.30 for the new integrated CHG-impregnated transparent dressing after 15 minutes of exposure for 12 of the 15 strains. Lesser reductions were seen with E. faecalis ATCC 29212 (2.18 log), E. faecium (VRE) ATCC 51559 (2.93 log) and M. luteus ATCC 7468 (0.22 log).

Study of Suppression of Regrowth on Prepped Subclavian Sites
At day 7, the new integrated CHG transparent dressing showed significantly lower regrowth post prep compared to the control (P<0.0001). At day 10, both CHG dressings showed significantly lower regrowth (P<0.0003). (Figure 5) There was a statistically significant difference between the new integrated CHG-impregnated transparent dressing and the CHG-impregnated sponge dressing at day 7 (∆ log$_{10}$ CFU 0.80, p<0.02).

There were no serious adverse events in the study, and all 3 dressings were well tolerated.

![Figure 5](image5.png)

FIGURE 5. Suppression of regrowth on prepped subclavian sites with the two CHG-impregnated dressings in healthy volunteers.

At day 7, the new integrated CHG transparent dressing showed significantly lower regrowth post prep compared to the control (p<0.0001). At day 10, both CHG dressings showed significantly lower regrowth (p<0.0003). There was a statistically significant difference between the new integrated CHG-impregnated transparent dressing and the CHG-impregnated sponge dressing at day 7 (∆ log$_{10}$ CFU 0.80, p<0.02).

![Figure 6](image6.png)

FIGURE 6. In Vivo time kill of normal flora on unprepped skin with the two CHG-impregnated dressings in healthy volunteers.

In Vivo Time Kill Of Flora On Unprepped Skin
A plot of the log$_{10}$ counts for the 20 subjects with paired data available at day 7 is provided in Figure 6. In comparing bacterial log reductions from baseline over time, the new integrated CHG-impregnated transparent dressing had directionally higher average log reductions compared to the CHG-impregnated sponge-disc dressing at each day, however, these differences only achieved statistical significance at day 1 and day 4 (day 1 ∆ log$_{10}$ CFU/cm$^2$ 0.60, and day 4 ∆ 0.80) (P=0.03;P=0.0008). The likelihood-based repeated measures analysis, which included both dressing and time in the model, showed the new integrated CHG-impregnated transparent dressing to be significantly more effective than the CHG-impregnated sponge dressing in reducing floral counts on unprepped skin across all time points (P=0.008); the result held whether the analysis was conducted on the available data only or on the data set where missing values were imputed using the non-missing values from a previous day by LCOF.

DISCUSSION

CHG has been used widely throughout the world for more than 50 years for cutaneous disinfection, hand hygiene and oral hygiene, and the safety of CHG is well established.$^{12}$ Clinically relevant high-level bacterial resistance has been very rare.$^{13-15}$

The Biopatch™ hydrophilic CHG catheter site dressing has been a technologic advance for prevention of CRBSI with short-term vascular catheters. Recent prospective randomized trials of the dressing have shown major reductions in catheter colonization and CRBSI,$^{9,10}$ but it is essential to apply the dressing properly if it is to be effective, with the CHG-impregnated side apposed firmly to the skin surface and the entire 360° circumference of the catheter protected, immobilized with a transparent polyurethane dressing (Figure 1). The dressing must not be simply laid on top of the catheter at the insertion site, which commonly occurs in clinical practice and greatly diminishes its efficacy.

In this study, the new integrated CHG dressing showed powerful bactericidal activity against diverse nosocomial microbial species, and both CHG dressings studied showed excellent immediate and, especially, long-term cutaneous floral suppression and were well tolerated. The new integrated transparent CHG-impregnated dressing is easier to apply and less vulnerable to improper application, reliably secures the catheter, permits continuous inspection of the insertion site, and obviates the need for every-other-day site care. It now warrants evaluation in a prospective randomized clinical trial to determine if it also can prevent catheter colonization and reduce the incidence of CRBSI.

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DISCLOSURE. Dr Maki holds no personal financial interest in the CHG dressings studied and has received no compensation for his participation in these studies.