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Comparison of Four Antiseptic Products Containing Chlorhexidine Gluconate

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The purpose of this study was to compare the antimicrobic efficacies of four formulations of chlorhexidine gluconate (CHG) for handwashing under frequent-use conditions. Fifty volunteers were assigned by block randomization to one of five products: one of two liquid detergents containing 4% CHG, a liquid detergent containing 2% CHG, a foam containing 4% CHG, and a nonantiseptic soap (control). Subjects washed their hands by a standardized technique 15 times per day for 5 days. After days 1 and 5 of handwashing, there was a significant reduction in log CFU for subjects using all four CHG-containing products compared with subjects using control soap and for subjects within each group after days 1 and 5 compared with the base-line CFU counts (all $P < 0.05$). There were no significant differences between the four CHG products at any testing time. We conclude that all four formulations are satisfactory for clinical use.

Chlorhexidine gluconate (CHG) is a Food and Drug Administration-approved antimicrobial agent for topical application in products designed for surgical hand scrub, health care personnel handwashing, and patient preoperative scrub (1). It has been available in the United States for more than a decade in a single 4% formulation, but more recently has become commercially available in a number of other formulations, including liquid and foam bases as well as 2 and 4% concentrations. Because the chemical activity of CHG can be markedly affected by variations in formulation and detergent base (2), this study was conducted to compare four of the currently marketed formulations of CHG in terms of antimicrobial efficacy and subject acceptability.

A careful analysis of the efficacy of antiseptics requires several steps. (i) In vitro and animal studies are conducted to demonstrate safety and antimicrobial activity. (ii) Organisms are artificially inoculated onto skin and harvested after application of test agents. (iii) Efficacy against normal and transient flora is tested under controlled conditions to isolate the independent effects of the agent (as opposed to the effects of potentially confounding variables such as quality or frequency of handwashing and degree of contamination of the hands). (iv) Products are tested in clinical settings to assess effectiveness in reducing nosocomial infections.

The purpose of this study was to compare the antimicrobial effectiveness of several formulations of a single antiseptic ingredient (step 3 above) and to answer the question, Are there differences in antimicrobial activity of several different formulations of CHG? It would not be possible to answer this study question under uncontrolled conditions in a hospital since we would not be able under those circumstances to control the frequency and technique of handwashing or the extent of exposure to other antiseptics, nor could we quantify the level of microbial contamination of the hands. Therefore, a carefully controlled design using human volunteers in a laboratory setting was chosen.

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MATERIALS AND METHODS

A convenience sample of 50 healthy adult volunteers with no history of allergies or sensitivity to topical soaps or detergents, psoriasis, eczema, or other skin diseases was recruited primarily from among employees and students at the study institution. All subjects gave informed consent and were remunerated for their participation.

Three days before the beginning of testing, subjects were instructed in a standardized 15-s handwashing technique and were required to demonstrate competence. Each individual was given a bottle of nonmedicated liquid soap (Ultra-Kind Gentle Wash, Sani-Fresh International, Inc., San Antonio, Tex.) to use throughout the testing period for general bathing and handwashing. This same soap was used by a control group during testing. Subjects were also provided with disposable plastic gloves and instructed to avoid hand contact with any soaps, detergents, lotions, and cleaning materials throughout the 3-day weaning period and the 5-day testing period. Rings and nail polish were not worn during the testing period.

Subjects were assigned by block randomization to one of five treatment groups: one of two formulations of detergent-based liquid containing 4% CHG (Bacto-Shield liquid [CHG4; Amsco, Erie, Pa.] or Hibiclens [CHG4a; Stuart Pharmaceuticals, Wilmington, Del.]), a detergent-based foam containing 4% CHG (Bacto-Foam; Amsco), a detergent-based liquid containing 2% CHG (Bacto-Shield 2 [CHG2]; Amsco), and the nonmedicated control soap.

The four liquid antiseptic products were dispensed in pumps that yielded 4 ml of product per handwash. The foam was dispensed in the palm of the hand; subjects were instructed to use a golf-ball-sized bolus. Since no pumps were available for control soap, it was dispensed in syringes so that subjects could measure 4 ml per wash. For 5 days, subjects washed their hands 15 times per day with the assigned product and using the standardized technique under supervision in a laboratory. Hands were dried after each wash with a paper towel.

TABLE 1. Results of handwashing with four CHG-containing products

Product group	Base-line CFU	Change in mean log CFU on hands after:			
		Initial wash	8 Washes	15 Washes	5 Days
CHG4	5.94 ± 0.51[a]	−0.34	−0.76	−1.31	−2.15
CHG2	5.67 ± 0.54	−0.07	−0.62	−1.14	−1.80
Foam	5.88 ± 0.49	−0.20	−0.88	−1.24	−1.83
CHG4a	6.28 ± 0.60	−0.88	−1.16	−1.64	−2.36
Control	5.89 ± 0.47 (P = 0.09[b])	−0.11 (P = 0.92[b])	−0.59 (P = 0.43[b])	−0.85 ($P < 0.05$[c])	−0.59 ($P < 0.001$[c])

[a] Mean ± standard deviation.
[b] Analysis of variation, comparing difference between treatment groups at each sampling time.
[c] Difference between control and other products statistically significant, but no significant difference between the four antiseptic products.

The two outcomes of interest were changes in quantity of bacterial flora colonizing the hand and subject assessments of their skin conditions and of the products tested. Samples from the skin of the hands were obtained for bacterial culture at five intervals: before the test period, but after a short handwash with nonantiseptic soap to remove contaminants (base line); three times on day 1 of testing (after washes 1, 8, and 15); and once on day 5 of testing (after the final wash). To obtain these samples, the subject inserted the dominant hand into a sterile polyethylene bag containing 50 ml of sampling solution (sterile distilled water containing [per liter] lecithin, 20 g; sodium thiosulfate, 6 g; sodium oleate, 6 g; protease peptone, 1 g; tryptone, 1 g; and Tween 80, 50 ml [pH 7.2 to 7.4]) (5, 6). In preliminary studies, we determined that there was no significant increase or decrease in CFU in the solution within the first 2 h after sampling. Sampling solution from a random sample of bags was also cultured at the beginning and end of the test period and found to be sterile.

For each subject, the surface of the hand was rubbed vigorously through the wall of the bag for 1 min. All specimens were plated within 1 h of sampling. A 0.2-ml volume of each serial dilution up to 10^{-3} was placed on Trypticase soy agar (BBL Microbiology Systems, Cockeysville, Md.) containing yeast extract (5 g/liter) and Tween 80 (1 ml/liter), incubated aerobically at 37°C for 48 h, and then incubated at room temperature for an additional 48 h. CFU were counted and reported as total counts per hand in $\log_{10}$ CFU.

An ordinal, 7-point scale was used by subjects to assess the appearance, intactness, moisture content, and sensation of the skin on their hands at base line and again after 5 days of handwashing. Subjects also rated the acceptability of the assigned product on a similar ordinal scale. In a previous study, we demonstrated a high correlation between subject assessment of skin changes due to frequent handwashing and objective physiologic measures of skin damage (4).

Analysis of variance was used to test the significance of differences in $\log_{10}$ CFU between the five treatment groups at base line, on days 1 and 5, and for each product over time. The Kruskal-Wallis analysis of variance was used to test the significance of differences between subject assessment of the skin and of product acceptability among treatment groups. A Tukey test for multiple comparisons was used (8), and a probability of $P < 0.05$ was considered statistically significant.

RESULTS

All 50 subjects completed the 5 days of testing. There were 42 women (84%) and 8 men (16%) with ages ranging from 20 to 54 years (mean, 30.6 ± 7.7). Mean base-line $\log_{10}$ CFU counts ranged from 5.67 to 6.28. Although subjects assigned to CHG4a had slightly higher CFU counts at base line than subjects assigned to the other four product groups, these counts were not statistically significant (P = 0.09). Mean CFU counts in all five treatment groups decreased at every testing interval, although reductions were very small in the control group (Table 1). There were no significant differences in CFU counts between any of the antiseptic soaps and the control soap after a single hand wash (P = 0.92) or after 8 washes (P = 0.43), but after 15 washes, reductions were significantly greater for all four antiseptic groups when compared with controls ($P < 0.05$). By day 5, subjects in all four antiseptic groups had statistically lower CFU counts than controls ($P < 0.001$) and counts that were significantly lower than at base line ($P < 0.001$). There were no significant differences in mean log CFU counts between the four antiseptic products ($P > 0.30$). In the five treatment groups, there were no significant differences in subject assessment of skin condition after the testing period (P = 0.78) or in product ratings (P = 0.69); all products were rated acceptable.

DISCUSSION

In addition to the antimicrobial efficacy of antiseptics (i.e., the extent to which they kill microorganisms when topically applied to the skin), there are two other characteristics which are important in the choice of handwashing agents. The first is how rapidly the active ingredient works. When an immediate reduction in the maximum number of CFU is desired, the alcohols continue to be the agents of choice for skin antisepsis (3, 7). As found in this study, a single application of CHG-containing products offers little advantage over plain soap in reducing colonizing flora.

A second characteristic of importance, referred to as substantivity or persistence, results when agents bind to stratum corneum and release their chemical activity over time (1, 2). The substantive effect of CHG became evident in this study after 15 hand washes for all formulations tested, and this effect is even more striking when CHG-containing products are compared with other antiseptics in long-term trials (4, 5). Thus, when continued chemical antimicrobial activity on the skin is desirable (e.g., during procedures requiring prolonged gloving or frequent contact with patients who have infections), CHG is an agent of choice.

Of particular interest in this study was the influence of various formulations of CHG on its effectiveness. Analysis of our data suggested that the formulas tested were comparable in effectiveness; all four CHG-containing products were significantly better than control soap and effected significant, sustained reductions in colonizing flora over base-line measurements. Although not significantly dif-

ferent, the reductions in flora among those using the 2% CHG product were less than those with any of the three 4% products. Given this high level of effectiveness and given the fact that an ideal level of reduction in colonizing flora on the skin of health care personnel has not been defined, other considerations such as cost and user preference are probably of equal importance when choosing among product formulations which are shown to be comparable. It is quite possible, for example, that with prolonged use (months to years), certain products will be found to be milder or more acceptable to users or to have other side effects which cannot be detected in a short-term study such as this one. This study represents an early step in product evaluation, that of describing antimicrobial efficacy and the comparability of various formulations.

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