

Comparison of a Waterless, Scrubless CHG/Ethanol Surgical Scrub to Traditional CHG and Povidone-Iodine Surgical Scrubs

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Abstract

A new waterless surgical hand scrub product containing 1% chlorhexidine gluconate (CHG) and 61% ethanol in an emollient-rich lotion base (CHG/ethanol-emollient hand preparation) was assessed. This clinical study was based on the Tentative Final Monograph for Health Care Antiseptic Drug Products¹ (TFM); Proposed Rule and ASTM E 1115-912, Standard Test Method for Evaluation of Surgical Hand Scrub Formulations.

A randomized, single center, blinded, well-controlled clinical study involving 124 healthy subjects evaluated the antimicrobial effectiveness in producing an immediate and persistent reduction in the normal bacterial flora of the hands. The CHG/ethanol-emollient hand preparation was applied without scrubbing or the use of water. The marketed products, 4% CHG (Hibiclens[®] Antiseptic Skin Cleanser) and 7.5% povidone-iodine (Betadine[®] Surgical Scrub), were applied using scrub brushes in two 3-minute or 5-minute surgical scrubs, respectively. Over a 5-day period, each subject performed a series of 11 surgical scrubs using one of the products. After the first treatment on Days 1, 2 and 5, surgical gloves were worn on one hand for 6 hours. Bacterial samples were taken using the glove juice technique at 1 minute and 6 hours after treatment.

The immediate bactericidal effect of the CHG/ethanol-emollient hand preparation after a single application resulted in a 2.8 log reduction in normal flora (compared to 1.1 log for Betadine Scrub and 1.2 log for Hibiclens cleanser). This bactericidal effect persisted throughout the study, and eventually increased to a 3.2 log reduction after the eleventh scrub on Day 5. The log reductions of the CHG/ethanol-emollient hand preparation proved to be significantly better ($p < 0.0001$) than that of Hibiclens cleanser at each sampling interval on Days 1 and 2, and of Betadine scrub at all sampling intervals.

Introduction

This poster describes the results of a clinical study designed to determine the antimicrobial effectiveness of CHG/ethanol-emollient hand preparation using the log reduction criteria for bacterial counts on the hands defined by the Food & Drug Administration's (FDA) Tentative Final Monograph for Health-Care Antiseptic Drug Products (TFM). In this trial, CHG/ethanol-emollient hand preparation is compared with two marketed products: Hibiclens cleanser (Stuart Pharmaceuticals, Wilmington, DE) containing 4% CHG in a detergent base, and Betadine scrub (Purdue Frederick Co., Norwalk, CT) containing 7.5% povidone-iodine in a detergent base. Changes in baseline skin condition were also measured based on results of subject self-assessment questionnaires.

Objectives

- To evaluate the effectiveness of the CHG/ethanol-emollient hand preparation as a surgical hand scrub based on the TFM criteria for immediate and persistent reduction in the number of bacteria on the hands.

- To assess the bacterial reductions achieved within 1 minute and at 6 hours post-treatment, comparing the CHG/ethanol-emollient hand preparation versus Hibiclens cleanser and Betadine scrub:
- To compare the hand skin condition resulting from the use of the CHG/ethanol-emollient hand preparation, Hibiclens cleanser and Betadine scrub based on subject self-assessment.

Methods

Study Design

A prospective, randomized, partially-blinded, parallel-group trial:

- 14-day pretreatment washout period for stabilization of hand bacterial flora, during which subjects refrained from using any topical antimicrobials, systemic antibiotics, or medicated soaps, lotions, shampoos, etc.
- 5 to 7 days of baseline bacterial evaluations where three baseline samples of hand bacterial flora were taken.
- Subjects with baseline bacterial populations $\geq 1.0 \times 10^5$ colony forming units (CFU) per hand at the first and second baseline samplings were eligible to be enrolled in the treatment period.
- 5-day treatment period during which subjects performed a series of 11 simulated surgical hand scrubs using one of the test products as follows:
 - Once daily on Treatment Days 1 and 5, and
 - Three times daily on Treatment Days 2, 3, and 4

Treatments

Subjects were randomized to receive one of the following three treatments:

- CHG/ethanol-emollient hand preparation (6 mL, 3 x 2 mL; until dry)
- Hibiclens cleanser (10 mL, 2 x 5 mL; 6 minutes)
- Betadine scrub (10 mL, 2 x 5 mL; 10 minutes)

Bacterial Samples

Bacterial samples were collected following scrubs on Treatment Days 1, 2 and 5.

Hands were randomized to bacterial sampling times. The first hand of each subject was sampled 1 minute after scrubbing. The second hand was then sampled 6 hours after scrubbing.

Sampling technique:

- Loosely fitting sterile surgical gloves were placed over the hands. Seventy-five (75) mL of sampling solution was aseptically added to the glove of the hand to be sampled at 1 minute.
- The glove was occluded above the wrist and the hand was uniformly massaged through the glove for one minute.
- After massaging, an aliquot of the fluid in the glove was aseptically transferred to a serial dilution tube containing suitable antimicrobial neutralizers to achieve a 1:10 dilution.

- Solutions were plated using Trypticase Soy Agar and incubated for 48 to 72 hours at 30°C ± 2°C. Colonies were counted and viable cells in the undiluted sample were calculated by standard methods.
- The second hand was sampled in the same manner at 6 hours after scrubbing.

Log reductions in bacterial counts were measured from samples collected at 1 minute and at 6 hours on Days 1, 2 and 5.

Reductions in bacterial counts achieved with CHG/ethanol-emollient hand preparation were compared with those of Hibiclens cleanser (a reference control) and Betadine scrub.

Parameter	CHG/ethanol-emollient hand preparation N=41	Hibiclens® Antiseptic Skin Cleanser N=41	Betadine® Surgical Scrub N=42
Age (years) Mean (SD)	39.0 (11.3)	40.6 (12.2)	38.6 (9.2)
Gender N (%)			
Male	3 (7)	9 (22)	7 (17)
Female	38 (93)	32 (78)	35 (83)
Race N (%)			
White	36 (88)	32 (78)	32 (76)
Black	4 (10)	7 (17)	6 (14)
Hispanic	1 (2)	1 (2)	-
Asian	-	1 (2)	2 (5)
Native American	-	-	2 (5)

Subjects

Healthy, male or female volunteer subjects, ages 18 to 65 years old, inclusive, with 1st and 2nd baseline counts $\geq 1.0 \times 10^5$ CFU per hand (Table 1).

Evaluation Criteria

Efficacy

Efficacy evaluations were based on the immediate and persistent activity of the CHG/ethanol-emollient hand preparation as measured by the log reduction from baseline counts per hand at 1 minute or 6 hours after the first scrub on Days 1, 2 and 5. The TFM criteria for the surgical scrub indication are:

- Day 1–1 log₁₀ reduction on each hand within 1 minute and the count does not exceed baseline within 6 hours.
- Day 2–2 log₁₀ reduction on each hand within 1 minute.
- Day 3–3 log₁₀ reduction on each hand within 1 minute.

Skin Condition

Subject self-assessment questionnaires were used at baseline and Day 4 to rate several skin characteristics (appearance, intactness, moisture content and sensation), based on a 7-point scale [1=abnormal (red, dry, itchy, etc.) to 7=normal].

Safety

Safety assessments were based on observed and reported adverse events.

Statistical Methods

Efficacy

- The microbial count from each baseline determination on each hand (CFU/hand) was converted to base 10 logarithms and then averaged to determine each hand's baseline count.
- Log reductions were calculated by subtracting the post-treatment log count from the average baseline log count on the same hand.

- The difference in log reductions at each time point, between the CHG/ethanol-emollient hand preparation group and each of the other two treatment groups, was assessed using a t-test. In order to maintain the overall rejection region at $\alpha=0.05$, a Bonferroni adjustment was made, with t-tests conducted at $p \leq 0.025$.

Skin Condition

- The change from baseline at Day 4 was calculated for each item on the subject self-assessment questionnaire.
- A one-way analysis of variance (ANOVA) on the rank-transformed change scores was used to test the effect of the formulation on each aspect of skin condition. If the overall effect was significant in the ANOVA ($p \leq 0.05$), differences between the treatments were tested with a multiple comparisons t-test at $p \leq 0.05$.

Results

Efficacy

The CHG/ethanol-emollient hand preparation group showed statistically significant reductions from baseline bacterial counts at all time points and exceeded the TFM criteria at the specified time points (Table 2). Hibiclens cleanser met the TFM criteria on Days 1 and 5 but not on Day 2. Betadine scrub failed to meet the TFM criteria at all time points except the 1-minute sampling following Scrub 1 on Day 1.

Date/Time point	CHG/ethanol-emollient hand preparation	Hibiclens® Antiseptic Skin Cleanser	Betadine® Surgical Scrub
Baseline Period Mean	6.3	6.3	6.3
Day 1 Log Reduction			
1 minute	2.8**	1.2	1.1
6 hours	2.9**	1.4	0.0
Day 2 Log Reduction			
1 minute	2.9**	1.8	1.4
6 hours	3.1**	1.7	0.4
Day 5 Log Reduction			
1 minute	3.2*	3.4	2.0
6 hours	3.2*	2.9	0.4

* Statistically significantly higher for CHG/ethanol-emollient hand preparation than for Betadine® Surgical Scrub.

** Statistically significantly higher for CHG/ethanol-emollient hand preparation than for Betadine® Surgical Scrub and Hibiclens® Antiseptic Skin Cleanser.

CHG/ethanol-emollient hand preparation had statistically significantly greater log reductions in bacteria at all time points when compared to Betadine scrub, and at all time points on Days 1 and 2 when compared to Hibiclens cleanser.

Skin Condition

On average, skin condition worsened in the Betadine scrub and Hibiclens cleanser groups for all four characteristics assessed. Skin condition improved or stayed nearly the same for all four characteristics assessed in the CHG/ethanol-emollient hand preparation group. Statistically, pair-wise comparisons showed significant improvements in the CHG/ethanol-emollient hand preparation group as compared to Hibiclens cleanser in all assessments. Compared to Betadine scrub, there were statistically significant improvements in Appearance, Moisture Content and Sensation. Overall, these results indicate the use of CHG/ethanol-emollient hand preparation resulted in better skin condition than the comparative products, Betadine scrub and Hibiclens cleanser.

Safety

One serious adverse event considered “probably not related” and one adverse event which was “not related” occurred during the study in the Hibiclens cleanser group:

- One subject experienced tachycardia considered “probably not related” to use of the product since it was a pre-existing condition.
- One subject had an inflicted injury considered “not related” to use of the product.

Three subjects reported adverse events in the CHG/ethanol-emollient hand preparation group, which

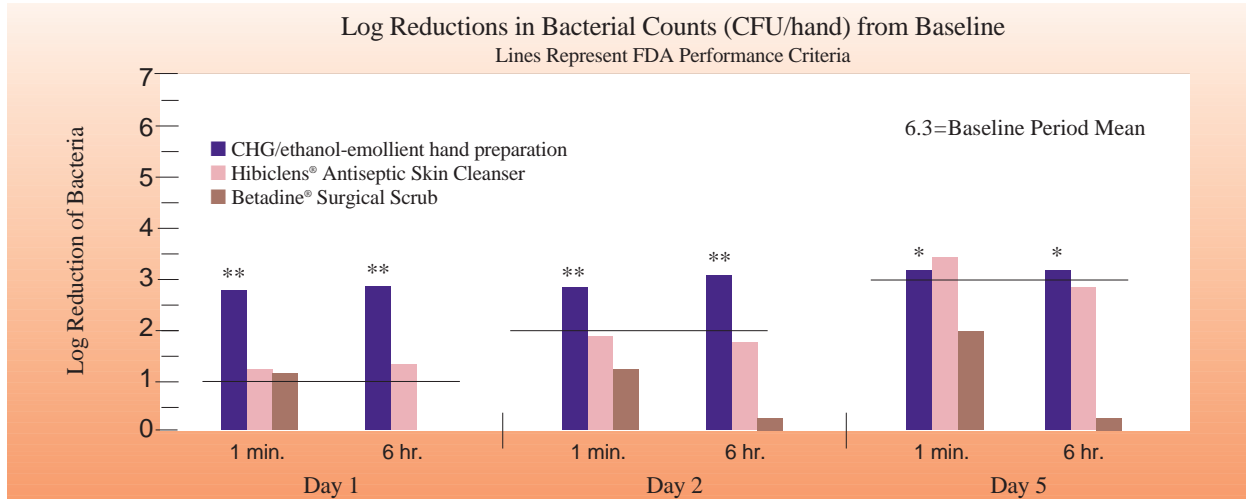
were “not related” to the study formulation:

- One subject with bronchitis
- One subject with inflicted injury
- One subject with vomiting

Three subjects reported adverse events in the Betadine scrub group which were “probably related” and “possibly related” to the product:

- One subject with papular rash and erythema
- One subject with papular rash
- One subject with erythema

Figure 1: Log Reductions in Bacterial Counts



*Statistically significantly higher for CHG/ethanol-emollient hand preparation than for Betadine® Surgical Scrub.

**Statistically significantly higher for CHG/ethanol-emollient hand preparation than for Betadine® Surgical Scrub and Hibiclens® Antiseptic Skin Cleanser.

Conclusions

- CHG/ethanol-emollient hand preparation exceeded the TFM criteria for antimicrobial effectiveness.
- CHG/ethanol-emollient hand preparation was equal or superior to Hibiclens cleanser in antimicrobial effectiveness, as assessed by log reductions in counts of hand bacteria.
- CHG/ethanol-emollient hand preparation was superior to Betadine scrub in antimicrobial effectiveness, as assessed by log reductions in counts of hand bacteria.
- CHG/ethanol-emollient hand preparation resulted in better skin condition than Betadine scrub or Hibiclens cleanser.
- CHG/ethanol-emollient hand preparation was well-tolerated.

References

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