

Population kinetics of the skin flora under the glove following surgical hand disinfection with three propanol-based hand rubs – a prospective, randomized, double-blind trial

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Population kinetics of the skin flora under the glove follow-up with three propanol-based hand rubs – a prospective, randomized trial

Abstract

Background and Objectives: The new CDC guideline for hand hygiene recommends either to use an antimicrobial soap or an alcohol-based hand rub supplemented with agents conferring persistent activity for surgical hand antisepsis. The most common agent which is thought to offer this latter type of effect is chlorhexidine gluconate. However, although often claimed, this effect has, to the best of our knowledge, never been adequately confirmed in a randomized, double-blind controlled trial.

Methods: Following a 3-min surgical hand disinfection with three propanol-based hand rubs, with or without agents believed to confer a persistent effect, and a 1-propanol 60% (v/v) reference, the population kinetics of re-growth of the skin flora under the glove have been studied at post-treatment times of 0, 1, 3 and 6 hrs in a prospective, randomized, double-blind trial with 24 adult volunteers. A slightly adapted version of the standardized European test method EN 12791 has been used in a Greco-Latin square design such that after eight experiments each subject had tested every formulation at the four sampling times making use of the split-hands model. An ANOVA applied to the lg PRE-treatment values did neither indicate any significant differences of the means obtained from left and right hands nor of those from the 8 experiments of the trial.

Results: Equivalence testing of the immediate bactericidal effects revealed that the blinded formulations A (1-propanol 60% v/v) and C (2-propanol 45% g/g plus 1-propanol 30% g/g plus mecetronium etilsulfate 0.2% g/g) were clearly equivalent to the reference, R, whereas that of B (2-propanol 70% g/g plus chlorhexidine gluconate 0.5 g/g) was questionable. The observed population kinetics of the skin flora proceeded as a very strong and fast initial reduction of the bacterial release from the fingertips by 2.7 lg with B and 3.5 lg with C. A and R caused intermediate reductions of 3.1 and 3.4 lg respectively, followed by slow re-growth as indicated by decreasing reductions. They did not reach 0, and were even after 6 hrs still significantly ($p < 0.01$) 0.9 to 1.5 lg below baseline. The slowest regrowth after 1 and 6 hrs was seen with C (Δ to 0 and 3 hrs = 0.1 lg and 0.7 lg, respectively). After 6 hrs, the slowest regrowth was observed with B (Δ to 0 hr = 1.6 lg).

Conclusions: Persistent activity of surgical rubs can not be easily shown if they meet the requirement of EN 12791 to exert an immediate effect equivalent to that of the surgical hand rub procedure laid down there as a reference. All preparations containing a non-volatile active agent

caused a (non-significant) slower regrowth of resident hand bacteria than the pure 1-propanols. But the potential of some of such chemicals to cause skin irritation and to promote bacterial resistance should also be considered.

Introduction

The new CDC guideline for hand hygiene recommends either to use an antimicrobial soap or an alcohol-based hand rub supplemented with agents conferring persistent activity for surgical hand antisepsis [1]. The most common agent which is thought to offer this latter type of effect is chlorhexidine gluconate [2]. However, although often claimed, this effect has, to the best of our knowledge, never been adequately confirmed in a randomized, double-blind controlled trial. Furthermore, recent data suggest that the effect commonly believed to be attributable to the sustained activity of chlorhexidine gluconate on the skin, might also be explained by insufficiently neutralized bacteriostatic activity of the agent which, during the test, is carried-over together with sampling fluids to the counting plates [3]. It is well known that effective neutralization of chlorhexidine gluconate is difficult to achieve [4, 5], hence, the supposedly observed bactericidal activity must often be suspected as being only pretended.

We undertook a prospective, randomized, double-blind trial to study the immediate and persistent effects of a three-minute surgical hand rub by measuring the bacterial release at 0, 1, 3 and 6 hours after disinfection with three different alcohol-based formulations. One preparation consisted only of alcohol, the others contained chlorhexidine gluconate (CHG) or mecetronium etilsulfate (MES) as supplements thought to confer a sustained effect.

Method

Test products

Four preparations were used (Table 1). Preparation B was Hibistat (Regent Medical, Norcross, USA), preparation C was Sterillium (BODE Chemie GmbH & Co. Hamburg, Germany).

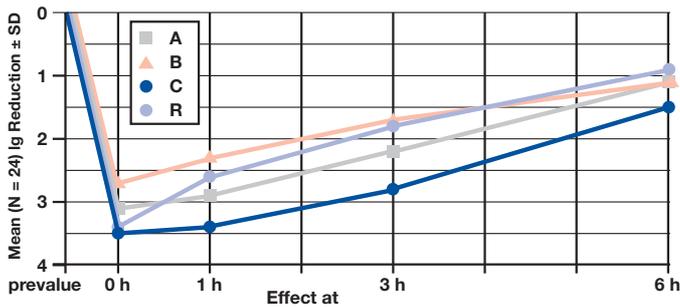
Design and randomization

For a total of 8 test runs, spaced from each other by one week, 24 volunteers were randomly allotted to the four hand rubs (including the reference) in four groups of 6 persons each and in sub-groups to the four sampling times. After the eighth run each volunteer had tested every preparation at every pre-determined time. All preparations were tested in parallel. To guarantee balance of the sequence of tests the four groups, four preparations, and four sampling times were arranged in a quasi-Greco-Latin square. The test method was that of EN 12791 but with 24 volunteers and with two additional sampling times (1 and 6 h).

Comparing surgical hand disinfection preparations in a randomized, double-blind trial

Code Preparation	Blinded	Type(s) and concentration(s) of active agent(s)
A	Yes	1-propanol 60% v/v
B	Yes	2-propanol 70%+CHG 0,5%
C	Yes	1-propanol 30%+2-propanol 45%+MES 0,2%
R	No	1-propanol 60% v/v

Table 1: Description of preparations



Code Preparation	Mean (N = 24) Ig Reduction ± SD			
	0 h	1 h	3 h	6 h
A	3.1 + 0.9 ¹⁾	2.9 + 1.2 ¹⁾	2.2 + 0.9	1.1 + 1.0 ³⁾
B	2.7 + 1.2*	2.3 + 1.1*	1.7 + 1.2*	1.1 + 0.8 ³⁾
C	3.5 + 1.2	3.4 + 1.1	2.8 + 1.3 ²⁾	1.5 + 1.0 ³⁾
R	3.4 + 1.0	2.6 + 1.3	1.8 + 0.8	0.9 + 0.7 ³⁾

* significant ($p \leq 0.01$) vs neighbor ²⁾ significant ($p \leq 0.01$) vs R
¹⁾ significant ($p \leq 0.01$) vs C ³⁾ significant ($p \leq 0.01$) vs PRE

Figure 1 and Table 2: Effects of three-minute applications of alcohol-based rubs on the microbial population kinetics on the hands

Test procedure

Hands were pre-washed with soap for 1 min. The bacterial pre-value was obtained by rubbing finger tips in tryptic soy broth (TSB) for 1 min. Subsequently, one of the surgical hand rubs was used applying a standardized rub procedure as described in EN 12791. After the end of the disinfection procedure, bacterial release from fingertips was, according to randomization, either obtained for immediate post-treatment values or hands were air-dried, gloved, and bacterial release obtained later after the pre-determined duration for (1, 3 or 6 hrs). At all of these occasions, the sampling fluids and their diluents contained neutralizer. The bacterial concentration in the sampling fluid was determined by serial dilution and surface culture.

Statistical evaluation

Mean Ig RFs with A, B or C derived from samplings 1 or 3 or 6 hours after disinfection were tested for significant differences to the corresponding means of R, first by the non-parametric Friedmann ANOVA and subsequently in pairwise post hoc comparisons by Wilcoxon-Wilcox-tests at p (one-sided) = 0.01. The Ig POST values at 6 hours were tested against the corresponding Ig PREs by Wilcoxon's matched-pairs tests.

Results

Immediately after disinfection, the reference disinfection had reduced the bacterial release from the fingertips by 3.4 ± 1.0 lg. Even 6 hours later, the bacterial density in the sampling fluid remained still 0.9 lg below baseline ($p < 0.01$). Similarly, the blinded n-propanol 60%-preparation, A, yielded comparable results at each sampling time. Preparation B (2-propanol 70% plus CHG) was somewhat less effective, especially at time 0, though never significantly. Preparation C (2-propanol 45%, 1-propanol 30% plus MES 0.2%) proved to be the most efficacious disinfectant at all sampling times, the differences of mean lg RF values reaching significance ($p \leq 0.01$) versus those of R at 3 hours, versus A at 1 hour and versus B at 0; 1 and 3 hours. At 6 hours, all preparations were still significantly ($p < 0.01$) below baseline.

The slowest regrowth after 1 and 3 h was seen with C (Δ to 0 h = 0.1 lg and 0.7 lg respectively). After 6 h, the slowest regrowth was observed with B (Δ to 0 h = 1.6 lg). Thus, with all preparations containing a non-volatile active agent a slower regrowth of resident hand bacteria was seen than with the rubs, A and R, containing solely 1-propanol.

Discussion

The immediate effect of the four preparations, as achieved within 3 min, was fast and strong. This is probably entirely due to the alcohols, the activity of which is positively associated (up to a certain limit) with their concentration, but also with the alcohol species with 1-propanol being the most active [6]. Therefore, it is not surprising that preparation C with its high total alcohol concentration (75%) and 1-propanol constituting 30% of the mixture causes the strongest reduction. This confirms the findings of others [7] who reported that among five surgical hand rubs formulation C was the only one the efficacy of which excelled that of the reference rub. In addition, it was reported recently that with hand rub C an application time of only 1.5 min was still enough to exceed the efficacy of the 3 min reference disinfection which confirms the superior performance of this formulation on the resident hand flora [8].

With regard to the 1-, 3- and 6-hours effects, it is interesting to note that preparations B and C containing CHG and MES respectively did cause some but, in this study, not significant persistent effects. A statement such as this should, however, be done with caution because the effects of both formulations were not compared to those of identical formulations not containing CHG or MES which limits the validity of respective conclusions.



→ Bacterial regrowth was slowest after 1 and 3 hrs with the formulation containing MES, and after 6 hrs with that containing CHG. Thus, it seems that MES and CHG do cause a certain persistent effect which, however, appears to be smaller than expected and reported earlier [2]. This rather low persistent effect may be due to more effective neutralization of CHG and MES in this study. And, indeed, it has been shown that in other studies ineffective neutralization of CHG may have produced false positive efficacy data [3].

It is notable that even at 6 hours the bacterial release from the fingertips was still significantly ($p < 0.01$) below the PRE-values by 0.9 to 1.5 lg. This signifies that bacterial re-growth under the surgical glove takes obviously more than 6 hours to reach baseline, if only the skin flora has been reduced strongly enough as has been achieved in this study with alcohols alone.

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