



## Letter to the Editor

# Effect on Skin Barrier and Usability of a Gentle 4% Chlorhexidine Hand Wash: A Prospective Randomized Controlled Trial

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### Abstract

**Background:** 4% Chlorhexidine has been the recommended antiseptic wash ingredient to be used in healthcare institutions to prevent healthcare-associated infections. However, at this concentration, it can be damaging to the skin barrier and can often cause or worsen hand dermatitis. We formulated a gentle 4% chlorhexidine hand wash using a mild amphoteric surfactant and the addition of humectants, such that the antiseptic wash will potentially be less damaging to the skin barrier and is user-friendly for healthcare workers. **Objective:** We aimed to compare the effect of the formulated gentle 4% chlorhexidine hand wash on the skin barrier with a standard antiseptic hand wash, and to evaluate its usability amongst healthcare workers. **Methods:** In phase one, a double-blinded randomized controlled trial was conducted at the National Skin Centre, Singapore. Eighty participants were randomized into two groups: gentle chlorhexidine hand wash versus a comparative 4% chlorhexidine wash that is currently used in many of Singapore's hospitals (Microshield® surgical hand wash, Schülke, Germany). The effect of the hand washes on skin barrier function was determined by measuring Trans-Epidermal Water Loss (TEWL) before and after handwashing. In phase two, all participants were provided with a 15ml fixed volume of the gentle chlorhexidine hand wash to use over 2 consecutive hours, and subsequently filled in a questionnaire that evaluates its usability. **Results:** The mean increase in TEWL after washing was lower in the gentle chlorhexidine hand wash group compared to Microshield® surgical hand wash but the difference was not statistically significant (25.8 g/m<sup>2</sup>/h vs. 31.4 g/m<sup>2</sup>/h; p=0.46). Subjective ratings of the gentle chlorhexidine hand wash were that it felt less drying, caused less skin sensitivity, had a nice texture and provided a feeling of cleanliness after washing. 60% of participants felt that it was overall better than their usual chlorhexidine hand wash. **Conclusion:** The formulated gentle 4% chlorhexidine hand wash showed a trend towards lower increment in TEWL after hand washing compared to the standard Microshield® wash. Subjective ratings indicated that the gentle chlorhexidine hand wash was well tolerated and usable.

## Introduction

The use of 4% chlorhexidine hand wash is the standard of care adopted by healthcare professionals [1]. However, at this concentration, it can damage the skin barrier and often causes or worsens hand dermatitis [2,3]. Occupational hand dermatitis has been cited as one of the top reasons for poor compliance to hand hygiene among healthcare providers [4,5]. The advent of chlorhexidine-based hand-rubs has helped to improve hand hygiene compliance but with respect to hand contact dermatitis, its role may be more harmful than beneficial [6,7]. Chlorhexidine based hand-rubs tend to impart an uncomfortable sensation of stickiness and subsequent washing of hands by users worsens the damaging effect on the skin barrier.

We formulated a gentle 4% chlorhexidine hand wash that aims to be less damaging to the skin barrier and yet possesses the antiseptic efficacy needed of a hospital-based hand wash. To achieve this, a mild amphoteric surfactant (lauramine oxide) that can be miscible with 4% chlorhexidine was used, and humectants (glycerine and allantoin) were added to the formulation. A series of *in vitro* anti-microbial tests were first performed, which demonstrated that the wash is 100% bactericidal against hospital pathogens like *Enterococcus hirae*, *Escherichia coli*, *Pseudomonas aeruginosa* and *Staphylococcus aureus*, and is virucidal against human coronavirus. A 21-day repeat patch test were subsequently performed in volunteers with sensitive skin which demonstrated the formulation to have a low level of irritation and sensitization potential, is hypo-allergenic, and is safe for use on sensitive skin.

The primary aim of this study was to compare the impact on skin barrier of the gentle 4% chlorhexidine hand wash versus a comparative 4% chlorhexidine wash that is currently used in many of Singapore's hospitals (Microshield® surgical hand wash, Schülke, Germany). The secondary aim of the study was to subjectively evaluate the usability of the gentle chlorhexidine hand wash among healthcare workers.

## Materials and Methods

Eighty healthcare workers at the National Skin Centre, Singapore, were enrolled for this two-phased study. In phase one, forty-one subjects were randomized into the gentle chlorhexidine hand wash group and thirty-nine into the Microshield® surgical hand wash group. Both the study investigators and participants were blinded to the interventions, with both washes being

contained in identical opaque bottles. Baseline trans-epidermal water loss [8] (TEWL) of the participants' left and right hands were measured using VapoMeter SWL5 from Delfin Technologies Ltd, Finland. They were then observed to wash their hands with the assigned washes, following the standardised World Health Organization (WHO) seven steps of handwashing [9]. TEWL was again measured after handwashing. At each TEWL measurement, three readings were taken on each hand and the average was calculated for each hand.

In phase two of the study, all the 80 participants were provided with a fixed volume (15 ml) of the gentle chlorhexidine hand wash. They were required to wash their hands using the gentle chlorhexidine hand wash over a consecutive two-hour work shift and had to finish using the entire volume of the wash. They were not allowed to use other hand washes, alcohol hand rubs or topical hand products during this two-hour period. Participants then answered a questionnaire to assess the usability and subjective impression of the gentle chlorhexidine hand wash.

The study was approved by the institution's ethics review board (reference number 2021/00181). Written informed consent was provided by all participants.

## Statistical analysis

Continuous variables were summarized as mean (SD) and categorical variables were summarized as numbers (percentage). TEWL was determined by taking the average score of the left and right hand. Change in TEWL was computed by subtracting each participant's TEWL score post-hand washing from their TEWL score pre-hand washing. Independent sample t-test was conducted to test for statistical differences in TEWL change between groups. ANCOVA was further conducted with post hand washing TEWL as the dependent variable and pre-hand washing TEWL as a covariate. All statistical analyses were conducted using SPSS (IBM SPSS Statistics for Windows, Version 24.0. Armonk, NY: IBM Corp). A p-value of <0.05 was considered statistically significant.

## Results

The participants' demographics in both groups were fairly uniform for gender, age and race. Majority of the participants in both groups washed their hands or used hand rubs 11 to 20 times in the course of their daily work. The most common reason for poor compliance to hand washing at work in both groups were that the washes were too drying (Table 1).

|   |                    | Gentle hand wash<br>(n=41) | %    | Micro shield hand<br>wash<br>(n=39) | %    |
|---|--------------------|----------------------------|------|-------------------------------------|------|
| <b>(A) Demographics</b>                                     |                    |                            |      |                                     |      |
| <b>Age, Mean (SD)</b>                                       |                    | 39.0 (12.4)                |      | 39.1 (10.9)                         |      |
| <b>Ethnicity</b>  | Chinese            | 39                         | 95.1 | 33                                  | 84.6 |
|   | Malay              | 1                          | 2.4  | 3                                   | 7.7  |
|   | Indian             | 1                          | 2.4  | 3                                   | 7.7  |
|   | Others             | 0                          | 0    | 0                                   | 0    |
| <b>Underlying atopy</b>                                     | Yes                | 3                          | 7.3  | 0                                   | 0    |
| <b>Hand dermatitis</b>                                      | Yes                | 2                          | 4.9  | 3                                   | 7.7  |
| <b>Use Topical steroids</b>                                 | Yes                | 1 (Mometasone cream)       | 2.4  | 0                                   | 0    |
| <b>Use Oral steroids</b>                                    | Yes                | 0                          | 0    | 0                                   | 0    |
| <b>Use Emollients</b>                                       | Yes                | 5                          | 12.2 | 0                                   | 0    |
| <b>Number of times of hand washing at work</b>              | <10x/day           | 18                         | 43.9 | 16                                  | 41.0 |
|   | 11-20x/day         | 18                         | 43.9 | 15                                  | 38.5 |
|   | >21-30x/day        | 5                          | 12.2 | 7                                   | 17.9 |
|   | >40x/day           | 0                          | 0    | 1                                   | 2.6  |
| <b>Number of times of alcohol hand rub at work</b>          | <10x/day           | 16                         | 39.0 | 14                                  | 35.9 |
|   | 11-20x/day         | 20                         | 48.8 | 15                                  | 38.5 |
|   | >21-30x/day        | 4                          | 9.8  | 7                                   | 17.9 |
|   | >40x/day           | 1                          | 2.4  | 3                                   | 7.7  |
| <b>What factors deter you from hand washing frequently?</b> | Sensitive skin     | 7                          | 17.1 | 9                                   | 23.1 |
|   | Soap too drying    | 21                         | 51.2 | 20                                  | 51.2 |
|   | Waste of resources | 3                          | 7.3  | 3                                   | 7.7  |
|   | Lack of time       | 13                         | 31.7 | 16                                  | 41.0 |
|   | Not Applicable     | 6                          | 14.6 | 5                                   | 12.8 |

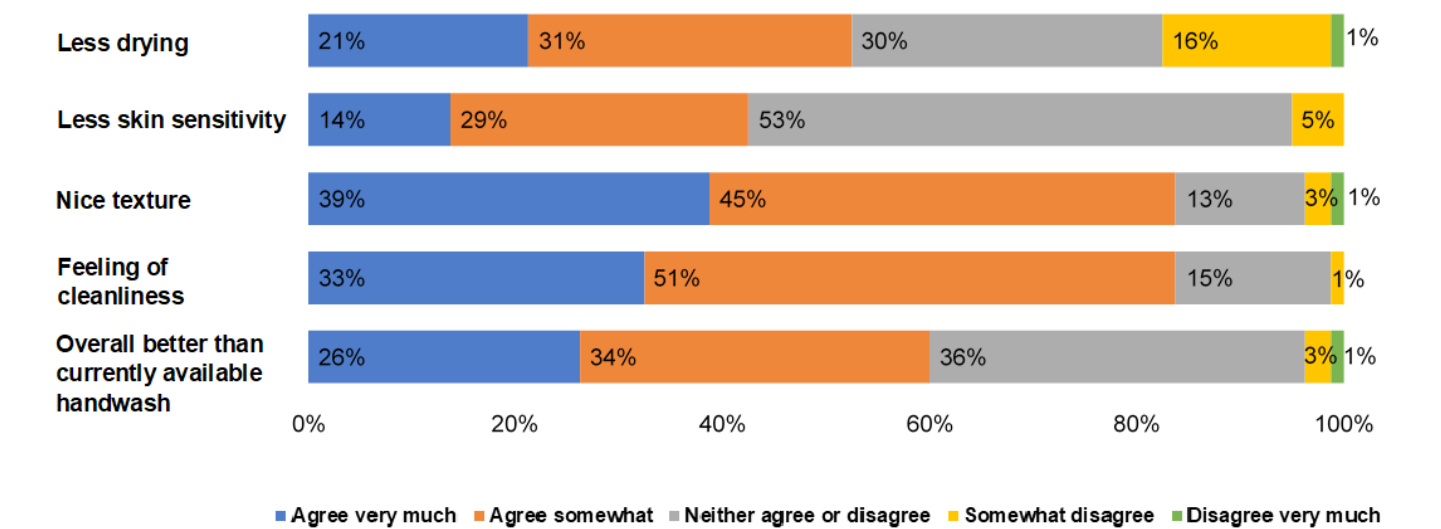
**Table 1:** Demographics and hand-washing practices of participants.

The increase in TEWL post-hand washing was lower in the gentle chlorhexidine hand wash group as compared to the Microshield® group (gentle wash=25.8 versus Microshield=31.4 g/m<sup>2</sup>/h); however, this difference was not statistically significant (p=0.46) (Table 2). Similar results were obtained after controlling for differences in pre-handwashing TEWL using ANCOVA (F(1,77)=0.41, p=0.52).

|   | Gentle hand wash<br>(n=41) | Micro shield wash<br>(n=39) | Mean Difference (95% CI) | P-value |
|---|----------------------------|-----------------------------|--------------------------|---------|
| Pre-handwashing TEWL  | 64.1 (42.9)                | 51.6 (34.2)                 |                          |         |
| Post-handwashing TEWL   | 89.9 (51.3)                | 83.0 (48.0)                 |                          |         |
| Change in TEWL <sup>1</sup>   | 25.8 (35.4)                | 31.4 (31.2)                 | 5.6 (-9.3 to 20.4)       | .46     |
| Mean (SD), trans-epidermal water loss (TEWL). <sup>1</sup> Change is calculated taking post-handwashing TEWL minus pre-handwashing TEWL for each participant. |                            |                             |                          |         |

**Table 2:** Trans-epidermal water loss of participants pre-and-post hand wash.

In phase two of the study, the gentle chlorhexidine hand wash was rated favorably in the subjective questionnaire. Eighty-nine percent (71/80) of participants rated the gentle wash as “good”, “very good” or “excellent”. Fifty-two percent (42/80) agreed that the gentle wash was less drying compared to the antiseptic wash they use normally. Forty-three percent (34/80) agreed that the gentle chlorhexidine wash caused less skin sensitivity, 84% (67/80) agreed that it had a nice texture, 84% (67/80) agreed that it provided a feeling of cleanliness, and 60% (48/80) agreed that it was overall better than current Microshield 4% chlorhexidine hand wash (Figure 1).



**Figure 1:** Results of questionnaire in phase two of the study that evaluated the usability of the gentle hand wash.

After all the participants had washed their hands using the gentle chlorhexidine wash in phase two of the study, 5% (4/80) experienced itchiness, dryness or tightness. Among the 80 participants, five had pre-existing hand dermatitis - none of them indicated that the gentle wash aggravated their hand dermatitis “extremely”, one indicated that the gentle chlorhexidine hand wash had “very much” aggravated his/her dermatitis, three indicated that the gentle chlorhexidine hand wash had “somewhat” or “slightly” aggravated their hand dermatitis, one participant indicated that the gentle chlorhexidine hand wash “not at all” aggravated his/her hand dermatitis.

**Discussion**

The prevalence of hand dermatitis in healthcare workers is two-fold [9] that of the general population [10]. It ranges between 16-30% (1-year prevalence) [9,11] and is one of the commonest reason for poor compliance [4,5] to hand washing in healthcare, thereby placing patients at risk of acquiring hospital related infections. This prevalent problem of hand dermatitis in healthcare workers have been exacerbated by the recent COVID-19 pandemic [12,13]. Surveys showed that approximately 25% of nurses reported existing symptoms or signs of dermatitis involving their hands, and as many as 85% gave a history of skin problems

involving their hands [14]. Frequent and repeated use of hand-hygiene products, particularly soaps and other detergents, are the most common cause for developing hand eczema in healthcare workers [15,16].

The choice of chlorhexidine at the concentration of 4% is chosen because of its bactericidal property and is considered standard of care in medical facilities, hospitals and clinics in Singapore [1]. However, the use of 4% chlorhexidine is damaging to the skin barrier and causes and aggravates hand dermatitis. Alternative hand wash solutions include octenidine, alcohol, triclosan and iodine. However, these hand washes have not been proven to be more favourable than 4% chlorhexidine. There is debatable effectiveness of octenidine as an antiseptic hand wash. Alcohol hand wash has poor activity against bacterial spores, protozoan oocysts and non-enveloped (non-lipophilic) viruses, in addition to being irritating and drying to the skin. Triclosan has not been approved by US Food and Drug Administration (FDA) for use as an antiseptic hand wash and iodine solution stains the skin yellow after repeated usage [18].

Our study showed a trend for the gentle chlorhexidine wash to be less damaging to the skin barrier, with a smaller increase in TEWL as compared to the Microshield® wash. The gentle chlorhexidine hand wash was well rated among the participants in terms of usability and likability. It was perceived to be less drying by majority of the participants, with a low number of participants experiencing irritation. As the study was conducted among healthcare workers instead of normal healthy volunteers, the results are more translatable to healthcare settings and clinical institutions.

There are a number of limitations in the study. Despite conducting the trial using a randomized controlled trial design, and taking the difference in the mean of three readings of TEWL, there was still significant intra and inter-individual variation in TEWL. These were possibly due to environmental and physiological factors that cannot be easily eliminated [18,19]. The exposure time that participants had with the gentle chlorhexidine hand wash was relatively short (two hours), and this may not provide a holistic evaluation of the cumulative effects of the gentle chlorhexidine hand wash on skin barrier. Future longitudinal studies with a larger population will allow for better evaluation of the effect of the gentle chlorhexidine hand wash.

## Conclusion

In summary, the formulated gentle 4% chlorhexidine hand wash showed a trend towards a lower increment in TEWL after hand washing compared to the Microshield® surgical hand wash. Subjective ratings indicated that the gentle chlorhexidine hand

wash was well-tolerated and highly usable. Development of antiseptic washes that are less damaging to the skin barrier can possibly aid in addressing the high prevalence of hand dermatitis, and improve hand-washing compliance among healthcare workers.

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## Ethics Statement

The trial protocols were approved by an institution review board: Doman Specific Review Board (DSRB) for National Healthcare Group (NHG), DSRB No. 2021/00348. Written informed consent was provided by all the patients.

## Conflict of Interest

The intervention for investigation was formulated by one the authors (H.L. Tey). The other authors have no conflict of interest to declare.

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