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Assessment of hand hygiene strategies on skin barrier function during COVID-19 pandemic: A randomized clinical trial

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Abstract

Introduction: Coronavirus disease 2019 (COVID-19) has increased the frequency of handwashing. There is scarce evidence regarding the impact of different hand hygiene procedures on skin barrier function in clinical practice.

Objective: To compare the impact on skin barrier function of different hand hygiene measures in healthcare workers in daily practice.

Methods: A randomized controlled clinical trial was conducted. Participants were randomized to sanitize their hands with water and soap, alcohol-based hand sanitizers (ABHSs), or disinfectant wipes during their 8-hour working shift. Epidermal barrier functional parameters, such as transepidermal water loss (TEWL), and the microbial load were assessed before and immediately after the working day. Tolerance and acceptability of each product were recorded after work.

Results: Sixty-two participants were included and 20, 21, and 21 were randomized to use water and soap, ABHS, and disinfectant wipes, respectively. After the 8-hour shift, TEWL increase was higher with disinfectant wipes than with soaps or ABHS (+5.45 vs +3.87 vs −1.46 g h^{-1} m^{-2}, respectively; $P = .023$). Bacteria and fungi colony-forming unit (CFU) count reductions were lower for the water and soap group than for ABHS and disinfectant wipes. Disinfectant wipes were considered more difficult to use ($P = .013$) compared with water and soap and ABHS.

Conclusion: Daily hand hygiene with ABHS showed the lowest rates of skin barrier disruption and the highest reduction of CFU.

KEYWORDS

COVID-19, hand disinfection, hand hygiene, hand sanitizers, skin barrier

1 | INTRODUCTION

The frequency of handwashing and disinfection has increased during the coronavirus disease 2019 (COVID-19) pandemic,[1] as it is believed that severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) can also be transmitted by direct and indirect contact.[2,3] For the required proper hand hygiene procedures,[4,5] currently there are several hand hygiene products available, such as soaps, alcohol-based hand sanitizers (ABHS), and disinfectant wipes.[6] ABHS reduce skin pathogens more efficiently[7,8] and, therefore, frequent application of ABHS containing at least 60% alcohol or, if unavailable, handwashing with a soap and water for at least

30 seconds, is recommended.[9,10] Nevertheless, a frequent use of these products may induce dry hands and skin damage, resulting in irritant or allergic contact dermatitis.[11] Moreover, injured skin is a potential host for SARS-CoV-2.[12]

Skin barrier impairment can be measured easily using objective parameters, namely, transepidermal water loss (TEWL),[13,14] the quantity of condensed water that diffuses across a fixed area of stratum corneum to the environment[13] which increases with barrier impairments,[15] stratum corneum hydration (SCH),[16] pH,[17] temperature,[18] and antioxidant capacity.[19] TEWL has been shown to increase with use of soaps[20] and to decrease with ABHS,[21] but there is only one study comparing the impact of different hand hygiene products on skin barrier function in the clinical practice.[22]

The main objective of this study is to compare the impact on skin barrier function of soaps, ABHS, and disinfectant wipes in healthcare workers (HCWs) in daily practice.

2 | MATERIAL AND METHODS

2.1 | Study design

An observer-blinded randomized comparative study following Consolidated Standards of Reporting Trials (CONSORT) guidelines (Supplementary Material) was designed and conducted between October 2020 and January 2021 in the Dermatology Department of the Hospital Universitario Virgen de las Nieves in Granada, Spain. Participants were HCWs, aged 18 to 60 years, who were randomized in a 1:1:1 ratio (computerized randomization) to use between every patient for hand hygiene, either washing with water and a soap, applying and rubbing their hands with an ABHS, or using disinfectant wipes for 20 seconds at least. Informative leaflets with rules for each procedure were delivered. Composition of each product is described in Supplementary Material. Intervention assignments were allocated by the study coordinator (S.A.-S.). The evaluator (T.M.-V.) was blinded to the assignments.

All participants were selected just at work arrival and included in the study after giving their written informed consent. After randomization, baseline measurements were taken at around 08:00 AM before participants had started their working shift, at least 30 minutes after any hand hygiene procedure. Participants were instructed on how to use only the allocated hand hygiene procedure, record the frequency of its application, and to avoid the use of protective gloves during the study and if gloves were worn, to take them off as soon as possible. After a full working day (around 03:00 PM), at least 5 minutes after the last hand hygiene procedure, microbiological samples were collected and, at least 30 minutes thereafter, skin barrier function parameters were measured.

Exclusion criteria were a previous personal history of any inflammatory skin disease, clinical infection of the area under evaluation, known or suspected incapacity to comply with the study protocol, or no signature on the informed consent form.

2.2 | Outcomes and measures

The primary outcome measure was skin barrier impairment, assessed by changes in TEWL, and secondary outcome measures were changes in temperature, SCH, erythema, pH and antioxidant capacity,[23] reduction of microbial load, as assessed by changes in bacteria and fungi colony-forming units (CFUs), and perceived differences in tolerability and acceptability[24] among the three hand hygiene procedures.

2.2.1 | Skin homeostasis and epidermal barrier function parameters

Before and after a working day, measurements were performed on the dominant palm after resting for at least 30 minutes in a room with controlled ambient air temperature and humidity, which were measured with the TFA Lab Thermometer IP65 LT-101 (Wertheim, Germany; average air temperature 22 ± 1°C; ambient air humidity 45% ± 5%). We used Tewameter TM 300 (Courage + Khazaka electronic GmbH, Bilbao, Spain) for TEWL ($g \cdot h^{-1} \cdot m^{-2}$), Corneometer CM 825 (Courage + Khazaka electronic GmbH) for SCH (arbitrary units (AU)), Skin-pH-Meter PH 905 (Courage + Khazaka electronic GmbH) for skin pH, Mexameter MX 18 (Courage + Khazaka electronic GmbH) for evaluating erythema index (AU), and Skin-Thermometer ST 500 (Courage + Khazaka electronic GmbH) for skin temperature (°C) connected to a Multi Probe Adapter (Courage + Khazaka electronic GmbH). All parameters were measured 10 times, and their average was used for analysis.

Total antioxidant capacity (TAC), for both fast antioxidants (Q1), which have a lower oxidation potential, and slow antioxidants (Q2),[23] was measured using the eBQC electrochemical method (Bioquochem S.L. [BQCkit], Asturias, Spain), and expressed in microcoulombs. Briefly, a conductive hydrogel, designed for direct measurement of the antioxidant capacity, is stuck to the skin surface and maintained in contact for 5 minutes and then peeled off and placed on the measurement area of the e-BQC strips.[23]

2.2.2 | Microbiological evaluation

At baseline and after the working day, microbiological samples were obtained by direct application of the four fingertips in a Petri dish with culture medium, either for bacteria (right hand) or for fungi (left hand). For bacteria, smears were placed in Trypcase Soy 3P Irradiated Trypcase Soy Agar (TSA3), a nonselective method, between 28 and 32°C for 72 hours and for fungi in Sabouraud Dextrose 3PTM Agar with irradiated neutralizers (SN3P) between 20 and 25°C for 96 hours. The composition of each medium is described in the Supplementary Material. The total number of CFU per plate were counted after 72 or 96 hours of incubation, and differences between baseline and end of the working day were used to assess the microbial load.

2.2.3 | Tolerability and acceptability

Tolerability and acceptability of the hand hygiene procedures were assessed after the working day using the protocol proposed by the World Health Organization (WHO) that allowed both objective evaluation by an observer and subjective evaluation by the participants.[24] Briefly, on a 7-point Likert scale, participants assessed the product's colour (unpleasant-pleasant), smell (unpleasant-pleasant), texture (sticky-nonsticky), irritation (very irritating-not irritating), drying effect (very much-not at all), ease of use (very difficult-very easy), speed of drying (very slow-very fast), application (unpleasant-pleasant), and overall evaluation (dissatisfied-satisfied). Likewise, on a 7-point scale, participants rated the skin condition of their hands: appearance (abnormal-normal), intactness (abnormal-normal), moisture content (abnormal-normal), sensation (abnormal-normal), and overall integrity of the skin (very altered-not altered). Skin condition was also assessed by the dermatologist evaluator as follows: redness (0-3, no redness-very bright with oedema), scaling (0-3, no scaling-very pronounced desquamation), fissures (0-3, no fissure-extensive cracks with bleeding or seeping), visual scoring of skin scale (0, no observable scale or irritation of any kind; 1, occasional scale that is not necessarily uniformly distributed; 2, dry skin and/or redness; 3, very dry skin with whitish appearance, rough to touch, and/or redness, but without fissures; 4, cracked skin surface but without bleeding/seeping; and 5, extensive cracking of skin surface with bleeding/seeping). All evaluations were carried out at baseline and after the working day using the hand hygiene product.

2.2.4 | Other variables

Sociodemographic data including sex, age, professional group (doctor, nurse, miscellaneous), work-related activities likely to cause skin damage and use of protective hand lotion/cream were recorded by a clinical interview. The phototype was assessed by a dermatologist using Fitzpatrick grading.[25] The frequency of hand hygiene procedures was self-reported by each participant.

2.3 | Statistical analysis

Participants were evaluated according to their randomized group using the intention-to-treat analysis. Descriptive statistics were used to present the sample characteristics. Continuous data were expressed as the mean (standard deviation, SD). The absolute and relative frequency distributions were estimated for qualitative variables. The Shapiro-Wilk test was used to check the normality of data distribution and Levene test to check the homogeneity of variance. One-way analysis of variance, post hoc Bonferroni correction, was used to compare quantitative variables between different hand hygiene procedure groups. The Student *t*-test for paired samples was used to compare differences in parameters before and after using the hand hygiene product. A linear regression model was constructed to evaluate variables associated with TEWL change. Epidemiological and statistical criteria were used to model variable selection. The effect of each exploratory variable on the model and its significance were studied. If the variable improved the model fit and adequacy (based on the likelihood ratio criteria and the significance of the parameter), it was kept; otherwise, the variable was excluded. The model was checked for pairwise interaction between covariates. Potential confounding covariates were studied using a change of significance in the model's parameters or a change of 30% of its value. Statistical significance was defined by a two-tailed $P < .05$. Statistical analyses were performed using the SPSS package (SPSS for Windows, version 24.0; SPSS Inc., Chicago, Illinois).

Accepting an α risk of 0.05 and a β risk of 0.2 in a two-sided test, 20 participants are necessary in each group to recognize as statistically significant a minimum difference of 6 units in TEWL between any pair of groups assuming that three groups exist. The common deviation is assumed to be 6. A dropout rate of 5% was anticipated. G*Power 3.1.9.2 (Heinrich-Heine-Universität, Düsseldorf, Germany) was used to calculate the sample size.

2.4 | Ethics

This study was approved by the Ethics Committee of Hospital Universitario Virgen de las Nieves on September 8, 2020 (HCHJ01/1489-N-20). The nature of the study was explained to all the participants, who agreed to participate by verbal and written consent. All measurements were noninvasive and participant data were kept confidential.

3 | RESULTS

3.1 | Baseline demographic and clinical characteristics

A total of 62 HCWs were included in the study: 20 of them in the water and soap group, 21 in the ABHS group, and 21 in the disinfectant wipes group (Figure S1). Only one participant did not finish the study. No significant differences in participants' demographic characteristics between groups were found (Table 1). The mean age was 38.32 (13.46) years and the female-to-male ratio was 1.48:1. Overall mean frequency of hand hygiene procedures was 8.52 (1.76) without differences between groups: 8.20 (1.32) times for water and soap, 8.43 (1.81) times for ABHS, and 8.90 (2.07) times for disinfectant wipes. Only two participants used protective gloves during the study (one in the AHBS group and another in the water and soap group) and the stated duration of wearing them was less than 5 minutes.

3.2 | Skin barrier impairment

TEWL increased by 5.45 (2.15) ($g\cdot h^{-1}\cdot m^{-2}$) in the disinfectant wipes group and 3.87 (1.71) ($g\cdot h^{-1}\cdot m^{-2}$) in the water and soaps group,

TABLE 1 Baseline demographic characteristics

Characteristic	All participants (n = 62)	Water and soap (n = 20)	Alcohol-based hand sanitizers (n = 21)	Disinfectant wipes (n = 21)	P-value
Age	38.32 (13.46)	39.20 (12.66)	36.43 (13.7)	39.38 (14.37)	.736[a]
Sex					.840[b]
Female	37 (59.7%)	13 (65%)	12 (57.1%)	12 (57.1%)	
Male	25 (40.3%)	7 (35%)	9 (42.9%)	9 (42.9%)	
Professional group					.693[b]
Doctors	34 (54.8%)	12 (60%)	11 (52.4%)	11 (52.4%)	
Nurses	6 (9.7%)	3 (15%)	1 (4.8%)	2 (9.5%)	
Miscellaneous	22 (35.5%)	5 (25%)	9 (42.9%)	8 (38.1%)	
Phototype					.394[b]
II	4 (6.5%)	0 (0%)	2 (9.5%)	2 (9.5%)	
III	57 (91.9%)	20 (100%)	18 (85.7%)	19 (90.5%)	
IV	1 (1.6%)	0 (0%)	1 (4.8%)	0 (0%)	
Nonwork-related activities likely to cause damage in skin (yes)	14 (22.6%)	5 (25%)	5 (23.8%)	4 (19%)	.889[b]
Use of protective hand lotion/cream					.831[b]
Several times/day	10 (16.1%)	4 (20%)	3 (14.3%)	3 (14.3%)	
Once/day	9 (14.5%)	3 (15%)	2 (9.5%)	4 (19%)	
Sometimes	13 (21%)	5 (25%)	3 (14.3%)	5 (23.8%)	
Rarely	7 (11.3%)	1 (5%)	3 (14.3%)	3 (14.3%)	
Never	23 (37.1%)	7 (35%)	10 (47.6%)	6 (28.6%)	

Note: Data are expressed as absolute (relative) frequencies or mean (standard deviation).
[a]*P*-value after using one-way independent analysis of variance, to compare differences in continuous variables between different hand hygiene products (water and soap, alcohol-based hand sanitizers, and disinfectant wipes).
[b]*P*-value after using chi-square test or Fisher exact test, as appropriate, was applied to compare categoric data between different hand hygiene products (water and soap, alcohol-based hand sanitizers, and disinfectant wipes).

whereas it was reduced by 1.46 (1.42) ($g \cdot h^{-1} \cdot m^{-2}$) in the ABHS group with significant differences between groups ($P = .020$; Table 2). Those using disinfectant wipes showed greater increases in TEWL values compared with those using ABHS ($P = .023$), but no statistically differences were observed between disinfectant wipes and soap or between soap and ABHS.

pH increased by 0.37 (0.12) in the water and soap group but remained unchanged in the ABHS group and the disinfectant wipes group. There were differences in pH changes between the three groups ($P = .014$), but the difference was only statistically significant when comparing the groups with soap and disinfectant wipes ($P = .014$).

Temperature decreased significantly by 1.62 (0.48)°C when using water and soap and by 1.73 (0.47)°C when using ABHS. TAC decreased significantly in all groups, for both fast and slow antioxidants. Fast antioxidant capacity decreased by 0.45 uC in the water and soap group, 0.25 uC in the ABHS group, and 0.25 uC in the disinfectant wipes group; and slow antioxidant capacity decreased by 0.86 uC in the water and soap group, 0.71 uC in the ABHS group, and 0.58 uC in the disinfectant wipes group. TAC decreased by 1.31 uC when using water and soap, by 0.96 uC when using ABHS, and by 0.86 uC when using disinfectant wipes. SCH and erythema did not change significantly in any group (Table 2).

A linear regression model was constructed to assess variables that could influence TEWL change (Table 3). After adjusting by type and number of the hand hygiene procedures in each working shift, temperature change, sex, and age, it was observed that water and soap ($\beta = 4.77$, $P = .05$), disinfectant wipes ($\beta = 6.14$, $P = .016$), and the temperature change ($\beta = 1.18$, $P = .015$) were independently associated with TEWL change.

3.3 | Reduction of microbial load

Percentage reduction in bacteria CFU count was lower in the water and soap group compared with those using ABHS or disinfectant wipes (65.7% vs 90.5% vs 87.44%, $P = .002$; Figure 1A). Moreover, percentage reduction in fungi CFU count was lower in the water and soap group than in those using ABHSs and disinfectant wipes (41.4% vs 80.3% vs 82.8%, $P = .017$; Figure 1B). No significant differences in fungi and bacteria CFU count reduction were observed between ABHS and disinfectant wipes groups, Figure S2.

TABLE 2 Changes in skin homeostasis and epidermal barrier function parameters

Skin homeostasis parameters	Water and soap (n = 20) Baseline (n = 20)	End (n = 20)	Change (n = 20)	*P*-value[a]	Alcohol-based hand sanitizers (n = 21) Baseline (n = 21)	End (n = 21)	Change (n = 21)	*P*-value[a]	Disinfectant wipes (n = 21) Baseline (n = 21)	End (n = 20)	Change (n = 20)	*P*-value[a]	*P*-value[b]
TEWL ($g \cdot h^{-1} \cdot m^{-2}$)	24.41 (7.55)	28.29 (11.81)	+3.87 (1.71)	.035	22.93 (7.41)	21.48 (8.15)	−1.46 (1.42)	.316	23.09 (9.67)	28.75 (14.16)	+5.45 (2.15)	.020	.020[c]
Scheme (AU)	44.14 (14.14)	40.85 (16.00)	−3.29 (2.03)	.122	46.60 (16.11)	43.26 (17.82)	−3.35 (1.99)	.109	44.33 (17.21)	45.20 (19.19)	+0.75 (2.43)	.760	.319
Temperature (°C)	28.94 (2.31)	27.32 (2.48)	−1.62 (0.48)	.003	29.70 (2.31)	27.97 (2.40)	−1.73 (0.47)	.001	29.58 (2.53)	29.58 (2.37)	−0.65 (0.49)	.230	.549
Erythema (AU)	238.40 (40.85)	224.04 (39.40)	−14.35 (8.73)	.117	253.19 (55.47)	251.40 (52.93)	−1.78 (6.82)	.797	251.47 (39.04)	263.81 (48.18)	+ 9.85 (5.60)	.095	.068
pH	6.31 (0.48)	6.68 (0.45)	+0.37 (0.12)	.005	6.57 (0.60)	6.51 (0.54)	−0.07 (0.17)	.685	6.85 (0.53)	6.64 (0.39)	−0.24 (0.14)	.116	.014[d]
Total antioxidant capacity (uC)	6.28 (1.51)	4.98 (1.15)	−1.31 (0.23)	<.001	6.82 (1.64)	5.86 (1.50)	−0.96 (0.42)	.033	6.64 (1.57)	5.75 (1.31)	−0.86 (0.29)	.009	.613
Fast antioxidant capacity (uC)	0.99 (0.45)	0.54 (0.19)	−0.45 (0.10)	<.001	0.97 (0.51)	0.72 (0.25)	−0.25 (0.13)	.062	0.90 (0.39)	0.65 (0.18)	−0.25 (0.08)	.004	.302
Slow antioxidant capacity (uC)	5.30 (1.23)	4.44 (1.00)	−0.86 (0.21)	.001	5.85 (1.30)	5.15 (1.29)	−0.71 (0.34)	.049	5.71 (1.25)	5.10 (1.19)	−0.58 (0.24)	.027	.762

Note: Data are expressed as mean (standard deviation).

Abbreviations: AU, arbitrary units; TEWL, transepidermal water loss, uC, microcoulombs.

[a] *P*-value after using Student *t* test for paired samples to compare parameters at baseline and after using the hand hygiene product.

[b] *P*-value after using one-way independent analysis of variance, post hoc Bonferroni correction, to compare changes in skin homeostasis parameters between different hand hygiene products (water and soap, alcohol-based hand sanitizers, and disinfectant wipes).

[c] Post hoc Bonferroni correction to compare changes in TEWL between soap and alcohol-based hand sanitizers ($P = .111$), between soap and disinfectant wipes ($P > .99$), and between alcohol-based hand sanitizers and disinfectant wipes ($P = .023$).

[d] Post hoc Bonferroni correction to compare changes in pH between soap and alcohol-based hand sanitizers ($P = .106$), between soap and disinfectant wipes ($P = .014$), and between alcohol-based hand sanitizers and disinfectant wipes ($P > .99$).

TABLE 3 Analysis of the factors related to transepidermal water loss changes

	Crude model			Adjusted model		
	β	95% CI	*P*-value[a]	β	95% CI	*P*-value[b]
Water and soap vs ABHS	1.97	−2.64 to 6.59	.395	4.77	0 to 9.55	.050
Disinfectant wipes vs ABHS	4.30	−0.20 to 8.80	.061	6.14	1.20 to 11.09	.016
Temperature change	1.36	0.14 to 1.30	.006	1.18	0.24 to 1.12	.015
Number of handwashings	−0.74	−1.98 to 0.51	.240	−0.80	−1.97 to 0.36	.171
Sex (female)	2.44	−1.95 to 6.82	.270	2.73	−1.39 to 6.85	.189
Age	0.095	−0.07 to 0.26	.240	0.01	−0.14 to 0.17	.873

Note: Data are expressed as mean (standard deviation).
Abbreviations: ABHS, alcohol-based hand sanitizers; CI, confidence interval; TEWL, transepidermal water loss.
[a]*P*-value after using a linear regression model to assess TEWL changes with one predictor.
[b]*P*-value after using a linear regression model to assess TEWL changes adjusted by the type of hand hygiene product (creating two dummy variables to compare water and soap vs ABHS and disinfectant wipes vs ABHS), temperature change, number of times of handwashing, sex, and age. β coefficient and 95% CI are shown.

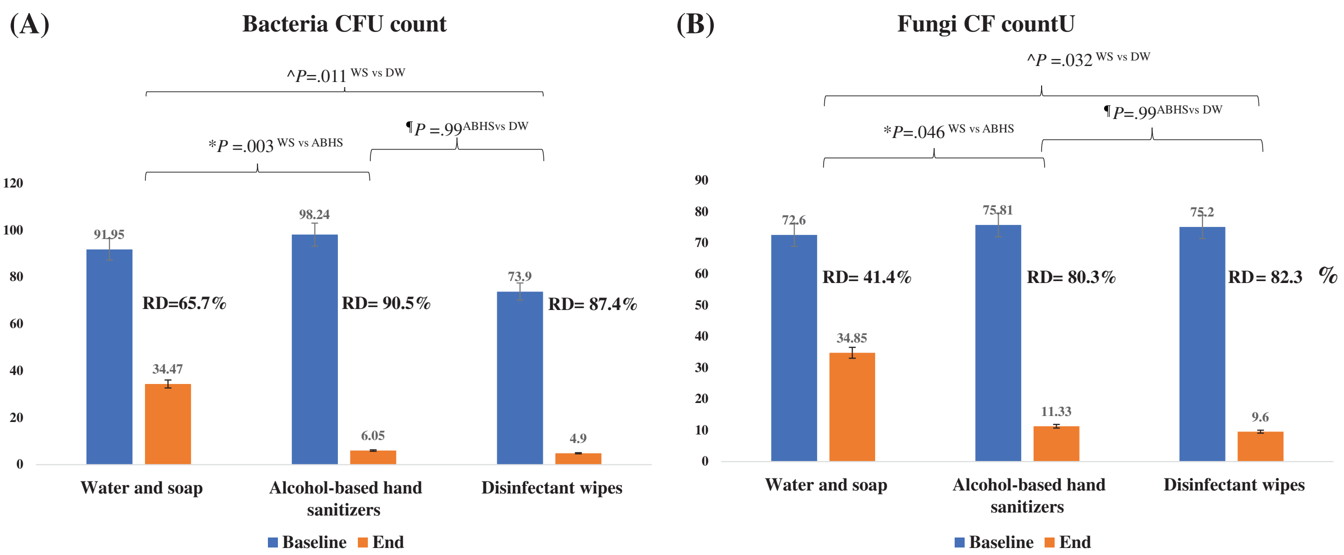

FIGURE 1 Reduction of microbial load. (**A**) Bacteria colony-forming unit (CFU) count reduction. (**B**) Fungi CFU count reduction. ABHS, alcohol-based hand sanitizers; ANOVA, analysis of variance; DW, disinfectant wipes; RD, percentage reduction in CFU; WS, water and soap

3.4 | Tolerability and acceptability

Differences were found in subjective evaluation of water and soap, ABHS, and disinfectant wipes regarding grading of colour ($P = .046$), drying effect ($P = .032$) and ease to use ($P = .013$), but not in other subjective parameters. The colour of disinfectant wipes was ranked lower than that of ABHS ($P = .047$). Disinfection wipes received worse ratings for the drying effect than ABHS ($P = .047$). Disinfectant wipes were less easy to use than ABHS ($P = .011$; Table 4). Regarding tolerability objective evaluation, differences in changes in redness (−0.05 vs 0.76 vs 0.95, $P < .001$) and changes in visual scoring of skin scale (−0.05 vs 0.71 vs 0.95, $P < .001$) were observed between water and soap, ABHS, and disinfectant wipes, respectively, whereas scaling or fissures were similar between groups. Changes in redness correlated with changes in erythema ($r = 0.38$, $P = .007$). Water and soap produced less redness than ABHS ($P < .001$) and disinfectant wipes ($P < .001$) with no differences between ABHS and disinfectant wipes.

4 | DISCUSSION

This study evaluated the impact of different hand hygiene procedures on the skin of the hands after a shift of 8 hours in HCWs, which is difficult to compare with other studies, which usually have this evaluation after longer periods and mostly in experimental settings, outside the regular work setting.[26,27] In our study we noticed that already after a single working day there were important differences between the three procedures of hand sanitation in almost all the parameters we evaluated (TEWL, CFU, and tolerability rates).

TABLE 4 Tolerability and acceptability of the hand hygiene products

	All participants (n = 62)	Water and soap (n = 20)	Alcohol-based hand sanitizers (n = 21)	Disinfectant wipes (n = 21)	*P*-value[a]
Subjective evaluation of the test product after using					
Colour (unpleasant-pleasant)	6.24 (1.15)	6.35 (1.04)	6.62 (0.67)	5.76 (1.48)	.046
Smell (unpleasant-pleasant)	5.95 (1.27)	6.35 (0.88)	6.05 (1.24)	5.47 (1.50)	.080
Texture (very sticky-not sticky at all)	5.16 (2.17)	4.75 (2.45)	4.86 (2.06)	5.86 (1.90)	.194
Irritation (very irritation-not irritating)	5.89 (1.67)	5.80 (1.96)	6.33 (0.86)	5.52 (1.94)	.284
Drying effect (very much-not at all)	3.66 (2.07)	4.15 (2.06)	4.24 (1.92)	2.71 (1.82)	.032
Ease to use (very difficult-very easy)	5.95 (1.67)	6.10 (1.48)	6.62 (1.16)	5.14 (1.98)	.013
Speed of drying (very slow-very fast)	4.85 (1.87)	4.15 (2.06)	5.24 (1.67)	5.14 (1.77)	.121
Application (very unpleasant-very pleasant)	5.97 (1.47)	6 (1.52)	6.24 (1.26)	5.67 (1.62)	.457
Overall evaluation (dissatisfied-very satisfied)	5.84 (1.35)	5.85 (1.27)	6.24 (1.13)	5.43 (1.54)	.150
Subjective evaluation of skin condition after using the product					
Appearance (abnormal-normal)	5.95 (1.66)	5.80 (1.79)	6.38 (1.07)	5.67 (1.98)	.342
Intactness (abnormal-normal)	6.56 (0.98)	6.60 (0.94)	6.60 (1.14)	6.48 (0.87)	.898
Moisture content(abnormal-normal)	5.77 (1.73)	5.45 (2.09)	6.48 (0.81)	5.38 (1.88)	.71
Sensation (abnormal-normal)	6.31 (1.39)	6.10 (1.71)	6.86 (0.36)	5.95 (1.56)	.075
Overall integrity (very altered- perfect)	6.39 (1.00)	6.25 (1.07)	6.67 (0.58)	6.24 (1.22)	.292
Objective evaluation					
Change in redness	0.56 (0.08)	−0.05 (0.05)	0.76 (0.12)	0.95 (0.12)	<.001
Change in Scaliness	0.10 (0.04)	0.05 (0.05)	0.20 (0.09)	0.05 (0.05)	.072
Change in fissures	0 (0)	0 (0)	0 (0)	0 (0)	1
Change in visual scoring of skin scale	0.55 (0.64)	−0.05 (0.22)	0.71 (0.56)	0.95 (0.59)	<.001

Note: Data are expressed as mean (standard deviation).
[a]*P*-value after using one-way independent analysis of variance to compare tolerability and acceptability between different hand hygiene products (water and soap, alcohol-based hand sanitizers, and disinfectant wipes).

Disinfectant wipes showed the highest TEWL increase. Water and soap also led to increased TEWL values, similar to disinfectant wipes. ABHS showed the best results, as it was the only hand hygiene procedure that did not increase TEWL values, likely in relation to lower skin barrier impairment. Previous studies showed that TEWL is increased by soaps[20] and is decreased by ABHS,[21] but it has been also stated that the skin barrier function is impaired by ABHS when applied on skin areas previously exposed to water immersion.[28] To our knowledge, the single previous study that assessed the impact of different hand hygiene procedures on skin barrier function in the clinical practice evaluated the effects of soap and water vs ABHS and showed no significant differences in TEWL changes.[26] Moreover, in experimental settings, with a lower participants number, ABHS caused less skin irritation and less skin barrier disruption than detergents.[27,29,30] ABHS and disinfectant wipes contain additional skin care substances, such as glycerine, a moisturizing agent, which may replenish lipids and trap water, improving epidermal barrier.[31] Moreover, cleaning hands with soap and water removes skin lipids as they are rinsed off, whereas they remain on the skin when using ABHS.[30] Lipids may be also potentially wiped off when using disinfectant wipes,[32] explaining their higher epidermal disruption compared with ABHS. Furthermore, the type of hand hygiene product was found to be an independent predictor for change in TEWL after adjusting for other variables, namely, gender and age, whose influence on TEWL is controversial.[32] Other factors, including the number of hand hygiene procedures and skin temperatures, which may have an impact on TEWL,[13] were similar in the three groups.

pH increase observed in the water and soap group may be explained by the alkaline pH of soap, or related to stratum corneum swelling, lipid rigidity, and skin irritation.[33] TAC decreased in all groups, for both fast antioxidants and slow antioxidants. TAC has been used as an inverse biomarker of oxidative stress, as it is an indicator of the sample ability to scavenge free radicals.[23] We used an electromechanical method to assess this parameter, which carries out a complete oxidation of the sample, considering individual peaks as the response of a specific antioxidant and obtaining the TAC measure through a mathematic algorithm. The total charge of antioxidants is divided into two sections: fast, including antioxidants with lower potential of oxidation, and slow, including antioxidants with higher potential of oxidation.[23] TAC predominantly measures chain breaking antioxidants, including uric acid and ascorbic acid, and excludes contribution of metal-binding proteins.[34] TAC decreased when using all hand hygiene products, which may be due to the reduction in biological and chemical antioxidant substances, such as gallic acid equivalents or vitamin C equivalents,[35] while the lack of differences between procedures could be because the increases in oxidative damage to lipids and proteins were not considered in this measure.[34] It would be interesting to use different measurements of individual antioxidants and markers of oxidative damage to accurately assess differences in antioxidant capacity between hand hygiene procedures.[34,36]

Regarding the antimicrobial power, water and soap showed the lowest reduction in bacterial and fungi CFU counts. ABHS and disinfect wipes had similar CFU reduction rates and both higher than water and soap. ABHSs kill microorganism by penetrating though their membrane and inducing cellular lysis, while soaps only remove debris from the skin.[31] Therefore, ABHS and disinfectant wipes may be more effective in reducing live bacteria and fungi that are able to form colonies in culture (reduced CFU) than water and soap, as shown in our study. Most studies observed higher rates of microorganism decontamination with ABHS[37] compared with soaps, including in the everyday use,[6,31] which is also in agreement with in vitro studies.[38] In agreement, WHO guidelines on hand hygiene in healthcare recommend using ABHS instead of water and soap if hands are not visibly dirty.[10] Viruses are more difficult to study in vivo and there are scarce studies that compare the viral load reduction with different types of hand hygiene products. In vitro, both soaps and ABHS are effective in inactivating enveloped virus.[39] ABHS also have a high activity against non-enveloped viruses.[10] Regarding disinfectant wipes, previously it has been observed that they are noninferior to water and soap[40] but less effective than ABHS[41] in reducing bacteria from the hands. These studies evaluated the antimicrobial power of the product after artificial contamination of the hands with *Escherichia coli*[40,41] while our study evaluated the effectiveness in removing usual microorganisms on the hand without any bacteria addition. The differences observed in the antimicrobial power between studies may depend on the predominant type of bacteria on the hand.

Hand hygiene products also have to be tolerable and acceptable to the user.[42] The lowest rating of tolerability and acceptability in this study was for disinfectant wipes, as they were considered as having the highest drying effect and being the least easy to use. Tolerability rates did not differ between ABHS and water and soap. Previous studies showed that ABHS are well accepted and tolerated among HCWs,[42] and during working hours they could be even more time-saving than water and soap.[43] There are no studies evaluating the tolerability of disinfectant wipes. In our study, the lowest rating of acceptability for disinfectant wipes might be explained by the fact that people are less used to employ them, and their application is more difficult and time-consuming than using a solution. Regarding tolerability objective evaluation, disinfectant wipes showed the highest rates for erythema increase, which might be explained by skin irritation.

This study has some limitations: (a) Only one type of hand hygiene product was tested in each participant; (b) The short follow-up, as the effect of the hand hygiene product, was evaluated after one working shift. Nevertheless, the assessment of skin barrier function parameters after only 1 day allowed to evaluate the overall impact of the hand hygiene products, as other factors, such as emollients use, could bias this effect. (c) Bacterial and fungal CFU were not differentiated. Therefore, we were not able to determine what type of product was most effective in eliminating the different types of microorganisms. (d) In contrast to most other studies, the palms and not the dorsum of the hands were selected for measuring the skin bioengineering parameters. The thicker stratum corneum of the palms may induce a distinct response to the hygiene procedures, but by contrast, the dorsum of the hands might be more influenced by external factors.[14] (e) There was a risk that evaporation of wash water was measured when assessing the TEWL. However, the 30-minute adaptation period before TEWL measurements reduced this possible bias.

5 | CONCLUSION

According to our findings, daily hand hygiene with ABHS showed the lowest rates of skin barrier impairment, the highest rates of CFU reduction, and was considered the most convenient and easy method to use.

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AUTHOR CONTRIBUTIONS

Trinidad Montero-Vilchez: Conceptualization (equal); data curation (equal); formal analysis (equal); investigation (equal); methodology (equal); writing – original draft (equal). **Antonio Martinez-Lopez:** Data curation (equal). **Carlos Cuenca Barrales:** Data curation (equal). **Maria Isabel Quiñones-Vico:** Data curation (equal). **Álvaro Sierra-Sánchez:** Data curation (equal). **Alejandro Molina-Leyva:** Supervision (equal); validation (equal); visualization (equal); writing – review and editing (equal). **Margarida Gonçalo:** Visualization (equal); writing – review and editing (equal). **Jacobo Jacobo Cambil-Martin:** Visualization (equal); writing – original draft (equal). **Salvador Antonio Arias-Santiago:** Conceptualization (equal); formal analysis (equal); funding acquisition (equal); investigation (equal); methodology (equal); supervision (equal); validation (equal); visualization (equal); writing – review and editing (equal).

CONFLICTS OF INTEREST

None declared.

DATA AVAILABILITY STATEMENT

Data available on request from the authors

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SUPPORTING INFORMATION

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