Adverse reactions associated with an alcohol-based hand antiseptic among nurses in a neonatal intensive care unit

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Background: Alcohol-based hand antiseptics are strongly recommended in the 2002 Centers for Disease Control and Prevention's hand-hygiene guideline. In a study comparing 2 hand-hygiene regimes, an alcohol-based (61% ethyl) antiseptic and a detergent containing 2% chlorhexidine gluconate in 2 neonatal intensive care units, we noted adverse reactions associated with the alcohol-based antiseptic.

Methods: A prospective study was conducted of the skin condition of 58 nurses using an alcohol-based product from March 2001 to January 2002. Adverse reactions to the alcohol-based product were noted and the Fisher exact test was used to determine factors associated with these reactions. Nurses with reactions to the alcohol product who were available to follow-up were patch tested to the product.

Results: Of 58 (1.1/100 nursing mo) nurses, 7 were evaluated by occupational health services for dermatologic symptoms that varied from mild to severe after use of the alcohol product, but 4 of 7 have resumed use. Nurses who had adverse reactions develop had been employed on the study unit and in the nursing profession for significantly less time than those with no reactions ($P = .037$ and $P = .002$, respectively), and were significantly more likely to report a history of itchy, sore skin ($P = .047$). A positive patch-test result was noted in 3 of 4 nurses with a previous reaction to the product.

Conclusion: This case series will alert users in the United States and elsewhere to the nature of reactions to alcohol products and how these reactions differ from reactions to traditional hand antiseptic products. (Am J Infect Control 2003;31:43-8.)

Waterless, alcohol-based products for hand hygiene in health care settings have been successfully used in some European countries for decades,[1] and are being increasingly adopted in the United States. In fact, the Centers for Disease Control and Prevention guideline for hand hygiene in health care settings highly recommends use of alcohol-based products for hand hygiene associated with most patient care encounters. In the course of a clinical trial comparing hospital-associated infection rates when either an antiseptic detergent or alcohol product was used for staff hand hygiene, we encountered several skin reactions to the alcohol product. The purpose of this study is to describe these skin reactions, compare them with typical reactions associated with traditional handwashing, and make recommendations for implementation and use of alcohol-based hand-hygiene products.

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METHODS

Sample and setting

The study was conducted on a 50-bed neonatal intensive care unit (NICU) in a hospital affiliated with a large academic health center in New York, NY. The NICU was selected because patients in the

Table 1. Characteristics of nurses with and without skin reactions

	Reactions (n = 7)	Nonreactions (n = 51)	*P* values*
Age (mean)	32.6	39.0	.11
Years as nurse (mean)	1.1	15.8	.002
Years on unit (mean)	3.7	11.9	.04
Hx itchy, sore hands	21.1%	2.9%	.047

*Mann-Whitney or Fisher exact test. *Hx*, history.

NICU are at high risk for infection,[2] patient contact is frequent, hand-hygiene requirements among staff are high, and the staff is relatively stable. Registered nurses who worked full time on the unit were invited to participate in a 2-year, longitudinal clinical trial using a crossover design to compare 2 hand-hygiene products. Although all staff and visitors to the unit were required to use the study product, nurses (and not physicians or other staff) were studied because they represent the only group who do not move from unit to unit and because they have the most frequent direct patient contact.

Procedure

From February 2001 to January 2002, the alcohol-based product (61% ethanol containing emollients) was provided to the unit in wall-mounted dispensers and individual pocket-size bottles along with a mild, nonantimicrobial soap to be used for soiled hands. No other hand-hygiene products were allowed. In addition, a mild lotion was available in dispensers. Nonlatex gloves were used throughout the study. In February 2002, a crossover was made and the alcohol product and mild soap were replaced by a detergent-based antiseptic soap containing 2% chlorhexidine gluconate (CHG). All other hand-hygiene products, such as gloves, were the same.

Participants completed an initial interview in which they reported their usual hand-hygiene practices and skin condition. Members of the research team randomly monitored practices on the NICU on day and night shifts throughout the entire study period. A member of the research team was present on the unit almost daily. Nurses hands were formally examined by a trained observer once a month and whenever there were potential skin problems.

If staff members had skin problems, they were referred to occupational health services if they deemed the problem serious. If a staff member had a reaction assessed by occupational health services to be sufficiently serious to warrant further follow-up, the person was either referred to the allergy clinic, provided with an alternative product for hand hygiene, or both. Whenever possible, a similar product of a different brand was substituted (ie, during the alcohol phase, an alternative alcohol product was provided; during the CHG phase, an alternative antiseptic detergent was provided).

Instruments

Two instruments were used to collect data on skin condition and hand-hygiene habits. The first was a demographic form, which included questions about skin condition, hand hygiene habits, and history of any skin problems. The second was a postcard-size diary card on which nurse participants were asked to record for 1 working shift/mo their hand-hygiene practices, including frequency of hand hygiene, lotion use, and gloving, along with the number of different neonates touched.

Patch testing

Nurses were patch tested for dermatologic reactions to the alcohol product if a skin reaction developed requiring treatment at occupational health services and were available for follow-up. In addition, comparison patch tests were performed on 2 nurses who worked on the study unit and did not have a skin reaction, and 2 nurses who did not work on the unit and were not routinely exposed to the product. Institutional review board approval was obtained and all participants signed an informed consent for the skin-patch test. Participants were instructed not to apply any products to the skin of the back for 72 hours before testing; and not to ingest antihistamines or anti-inflammatory agents, or to wash the area during the course of the test.

On day 1, 0.1 mL of the test product was applied to clean skin of the scapula and covered with nonstick telfa and occlusive dressing. The test site was examined on day 3 for erythema and papules, the same dressing reapplied, and on day 4 the site was re-examined. Results were read by a dermatologist and scored as recommended by the International Contact Dermatitis Research Group using a rating of negative, 1+ if erythema was present; and 2+ if both erythema and vesicles/papules or blistering were present.[3] The Fisher exact or Mann-Whitney *U* test was used to compare selected variables between those with and without reactions.

Table 2. Summary of skin reactions to date in neonatal intensive care unit hand-hygiene study

Age, ethnicity	No. times product used before reaction	Description	Allergies	Able to return to product?	Patch-test results description
26 y, White	Immediately on contact	Red, blotchy, itching, progressing to cracks and bleeding (Dx by OHS rash to hands)	History of eczema and asthma	Uses product sparingly	Negative
31 y, White	A "few times"	Fine white rash with red center, itching, evenly covered hands and wrists (Dx by OHS as irritant contact dermatitis)	History of eczema	Tried, but reaction recurred. Using another product (61% ethyl) with no problems.	2+ with blisters
21 y, White	Immediately on contact	Itching, progressing to dry, cracked bleeding areas. Eyes swollen and irritated (thought by OHS to be allergic reaction)	Amoxicillin, bee stings	No. OHS advised against use of other alcohol product; using CHG only	2+ with blisters
39 y, Asian	Immediately on contact	Itching progressing to excessive dryness; cracked, erythremic patches between fingers (Dx by OHS as irritant contact dermatitis)	Can not tolerate alcoholic beverages	Uses product sparingly	1+, raised erythema, no blisters

CHG, Chlorhexidine gluconate; *Dx*, diagnosed; *OHS*, occupational health services.

RESULTS

Of 58 full-time nurses employed on the study unit, 7 (1.1/100 nursing mo) were seen by occupational health services for skin reactions associated with the alcohol-based product; symptoms ranged from mild to severe during an 11-month period. This compared with 4/58 (1.0/100 nursing mo) reactions reported during a 7-month time period in the same unit when a traditional detergent-based antiseptic handwashing product was used. The signs and symptoms resulting from the alcohol-based product included red, itchy skin; erythema patches; and a rash that progressed to papules, blisters, and open lesions. Because of their severity, 2 nurses were instructed to replace the alcohol product with a detergent-based antiseptic containing CHG. A total of 5 nurses were given an alternative alcohol product to use and of these, 4 were able to resume use of the original alcohol-based product after several days. No reactions were noted among the neonates in this study who were touched by nurses using the alcohol product.

Nurses with reactions to the alcohol-based product were all female with a mean age of 31 years (range: 21-60 years). There were no significant differences between those with or without a reaction in ethnicity ($P = .11$) or use of lotion ($P = .52$). Those with reactions had been nurses for a significantly shorter period of time ($P < .002$), had worked on the unit for a significantly shorter period of time ($P = .04$), and were more likely to report a history of sore, itchy skin ($P = .047$) when compared with those without reactions (Table 1). Lost to follow-up were 3 nurses: 2 moved and 1 retired.

Patch-test results

The remaining 4 nurses with reactions and 4 comparison nurses were patch tested to the original alcohol-based product. The patch test was positive in 3 of the 4 nurses who had a reaction to the product and negative in all of the comparison nurses. See Table 2 for descriptive summary of the 4 nurses who presented with a reaction and were available for patch testing.

DISCUSSION

Review of literature

Contact dermatitis is an inflammatory disease of the skin with a clinical presentation of itching, redness,

Table 3. Characteristics of persons with topical reactions to waterless alcohol-based product and detergent-based antiseptics

Characteristic	Alcohol	Chlorhexidine
Onset	Immediate, soon after first use	After days or weeks of use
Description	Red, itching, and blistering	Extreme dryness, cracking, sometimes bleeding
Age	Usually young with shorter experience in health care	Usually older with long-term experience
Duration	Usually short term. Can often return to product after several days	Usually long term and worsening with use

and skin lesions that develop after contact with an irritant or allergenic chemical.[4] Irritant contact dermatitis results from exposure to an offending agent with resulting classic signs of skin irritation.[5] Cumulative irritant contact dermatitis is an acute manifestation of physiologic events that occurs after multiple exposures.[6] Clinical presentation of cumulative irritant contact dermatitis includes erythema, increased dryness and cracking of the skin.

Allergic contact dermatitis is a delayed immunologic response that arises after multiple exposures to an allergenic substance.[5] The skin of allergic contact dermatitis often is described as classic eczema with itching, plaques, papules, vesicles, and fissures.[5,6] Hand dermatitis among a group of hospital workers, 95% of whom were females, most often started on the fingers.[7] These health care workers reported a medical history of atopic symptoms and a family history of atopy that was statistically significant in the development of hand dermatitis. Hands are the most common site of dermatitis, and atopic dermatitis has been significantly associated with a history of dry, itchy skin; bronchial asthma and allergic rhinitis; a family history of atopic dermatitis; and female sex.[8]

Skin reactions associated with alcohols

A case of allergic contact dermatitis as a result of exposure to ethyl alcohol was reported in a 63-year-old man who received frequent venipuncture and presented with pruritic erythema to the antecubital area.[9] A dressing to the area contained 83% ethyl alcohol. The patient, who had a history of intolerance to oral and topical alcohol, had a positive patch test to ethyl alcohol at 15 minutes, 2 days, and 3 days. A 26-year-old furniture restorer presented with a 6-month history of eczema to the hands and forearms and was determined to have allergic contact dermatitis as a result of exposure to ethyl alcohol.[10] The dermatitis resolved when the patient stopped working, but symptoms reappeared on return to work. Patch testing with a standard series produced negative results, but patch tests with ethyl alcohol were all positive. A late-phase reaction to ethyl alcohol was reported in a 23-year-old female with a history of skin reactions to oral and topical alcohol.[11] Patch testing indicated that ethyl alcohol alone produced a positive reaction. The reaction was not noted before 3 hours, with peak reaction noted at 9 to 10 hours, and fading within 24 to 36 hours.

Rilliet et al[12] described the case of a 44-year-old Vietnamese midwife with contact urticaria syndrome. This patient experienced erythema after applying perfume or disinfecting her hands with alcohol, and headaches and dizziness after drinking small amounts of alcohol. In addition, she had rhinitis year round. Patch testing to alcohol was initiated and erythema was noted within minutes of applying ethanol to the forearm. Cases of pharmacogenetic, ethnic, nonimmunologic contact urticaria have been reported.[13] Three Asian participants who had severe facial flushing associated with oral alcohol were patch tested to aliphatic alcohols, aldehydes, and related chemicals. The results indicated a positive reaction to aldehydes and primary alcohols that can be converted to aldehydes.

Skin reactions associated with CHG

Both immediate and delayed hypersensitivity reactions associated with CHG have been reported.[14-16] In one 61-year-old man, both immediate and delayed hypersensitivity occurred simultaneously after surgical skin preparation with CHG.[17] Generalized urticaria has been reported after skin cleansing and urethral instillation of CHG.[18,19]

In 1989, Okano et al[20] reported 6 cases of anaphylactic symptoms confirmed by intradermal tests in persons aged 9 to 31 years after topical application. A similar series of 4 confirmed cases of CHG allergy with anaphylactic reactions was recently reported from Denmark.[21] Single case reports have occurred after application to intact skin or into the urethra.[22-25]

In our study 6 of 7 nurses with skin reactions to the alcohol-based hand antiseptic had dermatologic symptoms develop immediately on contact with the product. Each was evaluated at occupational health

services with similar symptoms that varied in severity. The 4 nurses with skin reactions to the CHG product gradually had dry, cracked skin develop during successive work days. None of the nurses in our study reported reactions to both the alcohol-based and CHG products.

Interpretation and conclusions

On the basis of our case series, it is neither possible nor appropriate to distinguish between an allergic and an irritant reaction, although the fact that 4 of the 7 nurses were able to resume use of the alcohol-based product argues against an allergic cause in those individuals. The reactions associated with alcohol were qualitatively different from those associated with traditional handwashing. They occurred in younger women, immediately or very soon after initial exposure to the product, and, in most cases, subsided within a few days so that the nurse was able to resume use of the product with no further problems.

The alcohol-based product used in this study was 61% ethyl alcohol with moisturizers. Earlier research by Held and Agner[26] reported that moisturizers do not necessarily protect the skin, but may actually increase the susceptibility of normal skin to an irritant. Further testing of the specific components of this alcohol-based product and their interaction may be necessary to determine the source of contact irritation.

Conversely, reactions associated with traditional handwashing generally occur after prolonged and frequent use of a product and are more common with older age as the skin becomes less resilient (Table 3). This dermatologic damage often becomes chronic and stubbornly resistant to treatment. Unfortunately, such irritant contact dermatitis associated with detergent-based products is extremely common, occurring in about one-fourth of full-time nursing staff.[27]

In summary, some adverse reactions to any product can be anticipated. In this series, reactions associated with alcohols differed from those associated with traditional handwashing in that they were more likely to include redness and blistering, but occurred earlier and less frequently and were associated with acute symptoms that often subsided. Hence, as health care facilities make the transition from traditional handwashing to use of waterless alcohol-based products, reactions can be anticipated, but are likely to be less common than with traditional hardwashing products. In several recent studies, use of alcohol-based products for acute care personnel has been consistently associated with improvements in skin health and improved compliance with hand hygiene when compared with traditional handwashing products.[28-33]

The purpose of this case series is to alert users to anticipate possible, albeit unlikely, reactions to any topical product applied to the skin. Further, the nature of reactions to alcohol products may differ from traditional handwashing and the reactions are likely to be short-lived. Although there may be the rare health care professional who can not tolerate alcohols, ultimately fewer skin problems may be anticipated when compared with use of antiseptic soaps or detergents.

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