American Journal of Infection Control 47 (2019) 933–937

Contents lists available at ScienceDirect

American Journal of Infection Control

journal homepage: www.ajicjournal.org

Major Article

Health care worker sensitivity to chlorhexidine-based hand hygiene solutions: A cross-sectional survey

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Key Words:
Nursing
Occupational allergy
Sensitivity
Hospital worker
Acute hospital

Background: Health service hand hygiene programs have seen widespread use of chlorhexidine solutions. Reports of both immediate and delayed hypersensitivity to chlorhexidine are increasing among health care workers. This study examined the prevalence of self-reported symptoms of sensitivity to chlorhexidine solutions among health care workers.

Methods: This study was a cross-sectional online anonymous survey of all workers at a single health service.

Results: Of the 1,050 completed responses, 76.3% were female, 35.3% were nurses and midwives, 28% were medical staff, and 8.7% were working in nonclinical areas. Over 95% used chlorhexidine-based hand hygiene products in their workplace. Nurses and midwives most frequently reported asthma (13.7%), contact dermatitis (27.8%), and previous testing for allergy to chlorhexidine (4.9%). There was a correlation between both the presence of atopy, eczema, or dermatitis and the self-reporting of dry skin, eczema, or dermatitis attributed to chlorhexidine use.

Discussion: Occupational chlorhexidine allergy is an important risk to health care workers. Self-reported symptoms of sensitivity to chlorhexidine solutions revealed high reported use and presence of skin symptoms among health care workers.

Conclusions: Screening programs need to identify nurses who develop chlorhexidine sensitivity due to occupational exposure. Strategies to mitigate risk should provide alternatives for those with sensitization.

Improving health professionals' compliance with hand hygiene guidelines is a national and international priority to reduce preventable harms in hospitals. Chlorhexidine is commonly used as a disinfectant in hand hygiene products in health care settings.[1,2] The inception of focused hand hygiene programs has seen the widespread use of chlorhexidine in health services. Correspondingly, there have been increasing reports of both immediate and delayed hypersensitivity to chlorhexidine, including dermatitis and allergic responses such as anaphylaxis.[3-10] Increased occupational use of hand hygiene products has raised the risk of hypersensitivity reactions similar to other occupational exposures, such as latex, although little has been published on the topic of chlorohexidine sensitivity despite being frequently raised theoretically as a significant risk.[7,11]

Chlorhexidine is an antimicrobial agent that has been available since the mid-1950s.[4,7] Since that time, a growing awareness of hospital-acquired infections that can be prevented by improved hand hygiene practices has resulted in increasing use of chlorhexidine-based products as hand hygiene solutions, preoperative skin preparations, medical instrument disinfectants, and mouth rinses.[1,2,4,7] The focus of recent government and health service policy on patient safety has further accelerated the roll-out of hand hygiene products in hospitals around Australia, with some health services opting for alcohol-based products containing chlorhexidine.[12]

The evidence for routine use of chlorhexidine as a hand hygiene method is mixed. Initial views originated with a number of limited studies that suggested a benefit of chlorhexidine over alcohol alone

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Conflicts of interest: None to report.

Ethics approval and consent to participate: Ethical approval was obtained from the ethics committee of the participating health service.

https://doi.org/10.1016/j.ajic.2019.01.006
0196-6553/

owing to its prolonged antimicrobial bacterial effect, postulated to be up to 6 hours postapplication.[13-16] An Australian study[14] reported that the use of a chlorhexidine and alcohol hand hygiene product resulted in a significant decrease in the hospital-acquired methicillin-resistant *Staphylococcus aureus* infection rate. However, in this study, the introduction of the chlorhexidine-based product coincided with a significant workplace campaign to encourage staff compliance with hand hygiene recommendations,[14] and therefore the results may not be attributable solely to the introduction of chlorhexidine. More recently, a US-based study that compared an ethanol-only product with ethanol plus chlorhexidine reported significantly lower aerobic bacterial counts on the hands of health workers in an intensive care unit, both immediately after use of the product and after spending time in intensive care unit common areas.[16] Alternatively, a 2017 study[17] and a review of published datasets suggested the addition of chlorhexidine to alcohol hand hygiene products offered no clear benefit and added potential risk.[18]

When first introduced into health care services, the sensitization rate to chlorhexidine was considered low.[4] However, the increasing use of chlorhexidine hand hygiene solutions in health settings has seen a corresponding increase in reports of hypersensitivity.[19-21] Hypersensitivity symptoms attributed to chlorhexidine can range from dermatitis and urticaria to asthma and, in rare instances, life-threatening anaphylaxis.[8,21,22] Research exploring how many exposures to chlorhexidine are required to induce sensitization has reported variable results. One article identified no chlorhexidine sensitization among 100 theater staff who had daily exposure to chlorhexidine-based products.[23] A more recent Australian study identified that 2% of health care workers and 3% of patients had evidence of contact dermatitis from chlorhexidine; however, this study did not explore other allergic presentations, such as asthma, urticaria, or anaphylaxis.[24] Because of the limited data on sensitization to chlorhexidine within the health care workforce, it is difficult to ascertain the true prevalence of sensitivity to chlorhexidine hand hygiene products.[23,25] However, skin prick and intradermal testing with 0.00002%-0.0002% chlorhexidine and radioallergosorbent technique IgE antibody testing have been useful in clinically confirming sensitivity to chlorhexidine.[9,21,23]

Among health care workers, literature suggests sensitivity to chlorhexidine has been examined in only small cohorts of hospital staff.[21,23] However, although nurses are the largest professional group in the health care workforce and the highest users of hand hygiene solutions because of their short and frequent patient interactions, the prevalence of sensitivity to chlorhexidine among this occupational group has not yet been examined. If sensitization rates are high among nurses, health care organizations may need to consider alternative products, as exposure may carry risk of reactions, including anaphylaxis.

The purpose of this research was to measure the prevalence of self-reported symptoms of atopy and sensitivity to chlorhexidine hand hygiene solutions among nurses and other health care workers in a large health service that primarily uses chlorhexidine-based hand hygiene products. It was expected this study would provide the foundation for a future study to examine sensitivity to chlorhexidine among those reporting atopy and symptoms. The primary research question was, what is the prevalence of self-reported symptoms of atopy and sensitivity to chlorhexidine hand hygiene solutions among health care workers in a health service that primarily uses chlorhexidine-based hand hygiene products? Secondary questions were (1) is the prevalence of self-reported symptoms of sensitivity to chlorhexidine among nurses different from other health care workers, (2) is the prevalence of sensitivity to chlorhexidine hand hygiene solutions associated with the frequency of exposure, and (3) do health care workers who report symptoms of sensitivity to chlorhexidine hand hygiene solutions also report atopy more frequently than those without sensitivity symptoms?

METHODS

Design and setting

A cross-sectional online prevalence survey was conducted in 2016-2017 at a large public tertiary health care network in Melbourne, Australia. The organization had transitioned to using chlorhexidine with evaporative alcohol hand hygiene products in 2006.

Sample

An anonymous online survey was sent via e-mail to all workers (approximately 17,439) at the health service. The survey was also advertised to those attending the organization's annual flu immunization program, as well as through organizational and discipline-specific online newsletters. The option to complete a paper version of the survey and return it via internal mail to a secure mailbox was also provided in wards and at the flu vaccine service. Consent was implied by completion of the online survey. Data were collected between December 2016 and June 2017.

Data collection tool

To measure sensitivity to hand hygiene solutions containing chlorhexidine, the Patient-Oriented Eczema Measure (POEM)[26,27] measured 7 symptoms of skin sensitivity using a 5-point scale of frequency of occurrence during the previous week, with a maximum total score of 28. The POEM tool was selected as a simple-to-administer self-report measure with previously established reliability and validity for the measurement of symptoms and sensitivity to change and differences between groups.[26,27]

Data analysis

Data were screened, cleaned, and examined for normality of distributions. The POEM tool was scored consistent with previous studies[26,27] and internal consistency examined using Cronbach α. Data collected using the POEM tool were analyzed using descriptive statistics. Independent group t tests and χ^2 tests were used to compare continuous and categorical variables, respectively. Significance was set at $P < .05$.

RESULTS

Characteristics of participants

Of the 1,112 responses, 65 incomplete surveys were removed, leaving 1,050 for analysis. Most respondents were female (76.3%) and employed as nurses and midwives (35.3%) or medical staff (28%). Small proportions were clerical (5.3%) and "other" staff, including managers, laboratory technicians, administrators, and project officers (6.6%). Of the respondents, 5.1% did not indicate their occupational group (Table 1). A small proportion of respondents (n = 192, 8.7%) worked in only nonclinical areas of the health service; many of those who reported working in nonclinical areas also worked in general wards (n = 70, 26.4%) or critical care settings (n = 40, 15.1%). Very few respondents reported they did not use chlorhexidine hand hygiene solutions in their workplace (Table 1).

Prevalence of self-reported symptoms of atopy

Participants were asked about symptoms of atopy they had experienced over the last year. Nurses and midwives most frequently reported asthma (13.7%), eczema (33.2%), and contact dermatitis (27.8%) independent of chlorhexidine when compared with other health care professionals, and also most often reported previous testing for allergy to

Table 1
Characteristics of respondents

N = 1,050	Nursing and midwifery	Medical	Allied health	Clerical	Other	Not specified
Participants n (%)	371 (35.3)	294 (28)	205 (19.5)	56 (5.3)	70 (6.6)	54 (5.1)
Estimated response rate*	5.4%	16.6%	35.5%	NA	NA	NA
Age mean (SD)	39.57 (12.15)	40.91 (12.28)	38.46 (10.8)	42.85 (12.77)	43.67 (13.2)	39.3 (13.28)
(n = responses)	(n = 357)	(n = 282)	(n = 200)	(n = 53)	(n = 69)	(n = 3)
Sex n (% female)	348 (93.8)	139 (47.3)	163 (79.5)	55 (98.2)	53 (75.7)	3 (5.6)†
Usual work environment:‡						
General wards	224 (60.4)	150 (51)	111 (54.1)	12 (21.4)	23 (32.9)	2 (3.7)
Critical care area (eg, ICU, NICU, ED, CCU, operating theater)	128 (34.5)	190 (64.6)	44 (21.5)	2 (3.6)	2 (2.9)	NA
Nonclinical or laboratory	40 (10.8)	40 (13.6)	97 (47.3)	45 (80.4)	42 (60)	NA
Do not use alcohol-based hand hygiene solution in the workplace	10 (2.7)	3 (1)	2 (1)	3 (5.4)	1 (1.9)	2 (2.9)

CCU, coronary care unit; *ED*, emergency department; *ICU*, intensive care unit; *NA*, not applicable; *NICU*, neonatal intensive care unit.
*Estimated total employees at time of survey conclusion: 17,439 (6,653 nurses, 216 midwives, 1,769 medical staff, 577 allied health staff).
†Fifty-one missing.
‡Participants may select more than 1 work environment.

chlorhexidine (4.9%). Of the nurses, 86.7% reported dry skin on exposure to chlorhexidine-based handrub, 73% reported developing a localized rash, and 20% reported developing respiratory symptoms. In comparison, only 6% of medical staff self-reported respiratory symptoms to chlorhexidine-based hand hygiene products (Table 2).

Prevalence of self-reported symptoms of sensitivity to chlorhexidine among nurses compared with other hospital workers

The POEM score[26] was used to measure severity of reported symptoms of sensitivity to chlorhexidine among health care workers. Of the 1,050 participants, 37% (n = 339) responded to all items on the POEM tool. Cronbach α of .82 demonstrated excellent internal consistency. Nurses had significantly higher ($P < .05$) scores for the POEM tool than medical, clerical, and other staff, but scores were similar to those of allied health staff (Table 3).

Association between prevalence of sensitivity symptoms and frequency of exposure

Only 1 respondent (nurse) reported anaphylaxis to chlorhexidine-based hand hygiene solutions. Nurses reported the most frequent use of hand hygiene solutions containing chlorhexidine during their workday compared with other health workers (Table 4).

The significance of associations between atopy and self-reported symptoms in response to chlorhexidine hand hygiene solutions was examined using χ^2 test for independence. The association between preexisting aero atopy (hay fever or asthma) and frequency of cough or wheeze symptoms in response to chlorhexidine hand hygiene solutions was nonsignificant. Important findings in relation to association between aero or skin atopy and frequency of symptoms in response to chlorhexidine included the following:

- Of those with self-reported aero atopy (hay fever or asthma)
  - There was no association between symptoms of cough or wheeze or widespread rash and chlorhexidine: 79.9% reported never experiencing any cough or wheeze.
  - 40.1% reported localized rash in the past year, including 33.3% who experienced localized rash every day ($P < .01$).
  - 36.6% reported eczema in response to chlorhexidine ($P < .05$).
  - 79.5% reported dry skin, 66% of these every day ($P < .01$).
- Of those with eczema or contact dermatitis
  - 89.8% reported dry skin, 74% of these every day ($P < .01$).
  - 63.4% reported eczema, 93.2% of these every day ($P < .01$).

Table 2
Self-reported symptoms present during previous year

	Nursing and midwifery	Medical	Allied health	Clerical	Other
Symptoms experienced	114 (30.7)	66 (22.4)	46 (22.4)	11 (19.6)	13 (18.6)
Atopic and asthma risk occurrence:					
Asthma	51 (13.7)	35 (11.9)	26 (12.7)	7 (12.5)	9 (12.9)
Hay fever	123 (33.2)	107 (36.4)	73 (35.6)	23 (41.1)	24 (34.3)
Aeroallergen	89 (24)	80 (27.2)	52 (23.5)	21 (30)	17 (24.4)
Eczema	62 (16.7)	36 (12.2)	34 (16.6)	7 (12.5)	9 (12.9)
Contact dermatitis	103 (27.8)	48 (16.3)	40 (19.5)	9 (16.1)	8 (11.4)
Skin allergen	134 (36.1)	67 (22.88)	57 (27.8)	14 (25)	16 (22.9)
Both skin and aeroallergen	56 (15.1)	41 (13.9)	29 (14.1)	5 (8.9)	8 (11.4)
Presence of allergy:					
Have an allergy	151 (40.7)	98 (33.3)	63 (30.7)	20 (35.7)	27 (38.6)
To food	45 (12.1)	18 (6.1)	20 (9.8)	6 (10.7)	11 (15.7)
To medications	82 (22.1)	39 (13.3)	34 (16.6)	9 (16.1)	16 (22.9)
Contact allergy	83 (22.4)	43 (14.6)	35 (17.1)	7 (12.5)	12 (17.1)
Other allergies	31 (8.4)	30 (10.2)	15 (7.3)	3 (5.4)	8 (11.4)
Have been tested for allergy to chlorhexidine	7 (4.9)	1 (1)	2 (3.3)	0	0
Symptoms regularly experienced in the last year related to chlorhexidine hygiene solutions:					
Dry skin	111 (86.7)	63 (75)	44 (21.5)	10 (17.9)	13 (72.2)
Eczema	39 (37.1)	20 (29)	19 (45.2)	1 (12.5)	5 (33.3)
Localized rash	55 (73.3)	21 (53.8)	15 (55.6)	3 (60)	6 (75)
Widespread rash	10 (9.9)	2 (3)	3 (7.9)	1 (12.5)	0
Wheeze/cough	21 (20.6)	4 (6.1)	7 (17.5)	3 (37.5)	2 (13.3)
Abdominal pain	11 (3)	1 (0.3)	8 (3.9)	0	0
Anaphylaxis	1 (0.3)	0	0	0	0

Table 3
Prevalence of self-reported symptoms of chlorhexidine sensitivity among hospital workers

	Nursing and midwifery N = 143	Medical N = 94	Allied Health N = 60	Clerical N = 17	Other N = 24
POEM score[26] mean (SD)	5.47 (5.39)	2.79 (4.55)	5.46 (5.28)	2.06 (3.21)	5.04 (6.54)
Mean rank	192.06*	129.94	190.78*	123.32	169.5

NOTE. POEM scores are 0-2 (clear/almost clear), 3-7 (mild), 8-16 (moderate), 17-24 (severe), and 25-28 (very severe).
POEM, Patient-Oriented Eczema Measure.
*Kruskall-Wallis test significant at $P < .05$.

- 62.5% experienced a localized rash, 100% of these every day ($P < .01$).
- There was no significant association between widespread rash and cough or wheeze.

- The presence of aero and skin atopy was strongly associated with frequency of skin symptoms, including exacerbation of eczema ($P < .01$).

Nurses who reported symptoms of sensitivity (dry skin, localized rash, widespread rash) to chlorhexidine hand hygiene solutions also reported atopy more frequently than nurses without sensitivity symptoms ($P < .05$).

DISCUSSION

Prevalence of self-reported symptoms of sensitivity to chlorhexidine among nurses and other health care workers

In this cohort of health care workers who responded to an anonymous questionnaire about sensitivity to chlorhexidine hand hygiene solutions, the rate of sensitization appears higher than that previously reported, at 23.8%. This is most likely related to a positive reporter bias, as those with symptoms of sensitivity would be expected to be more likely to complete the survey than those without. However, when the total number of hospital employees at the time of the survey is used as the denominator, this finding is on par with the background sensitization rate to chlorhexidine of 2.3% previously reported in the literature.[28] Despite the high rate of self-reported symptoms, only 1 report of anaphylaxis to chlorhexidine was identified, consistent with the findings of Garvey et al.[23] Approximately 250 health care workers at this organization reported symptoms related to regular use of chlorhexidine hand hygiene products. Of concern is the small number of health care workers reporting respiratory symptoms that they attributed to chlorhexidine-based hand hygiene products. This may impact on their compliance with hand hygiene practices and their quality of life.

Association between occupational exposure to chlorhexidine hand hygiene solutions and self-reported symptoms of sensitivity

Consistent with nurses reporting significantly higher ($P < .05$) scores for the POEM tool than medical, clerical, and other staff, over 70% of nurses reported using chlorhexidine-based hand hygiene products more than 20 times per shift compared with approximately 40% of medical and 20% of allied health staff. Similar to previous research, nurses reported the highest frequency of exposure to hand hygiene products and the highest frequency of work-related symptoms of sensitivity compared with other health professionals.[29] However, limited research specific to occupational exposure to chlorhexidine-based hand hygiene solutions and self-reported symptoms is available.

Health care workers' symptoms of sensitivity to chlorhexidine hand hygiene solutions and atopy

In comparison with studies of latex allergy, there was no correlation of symptoms to chlorhexidine exposure in staff who reported a background history of atopy with regard to the presence of cough or wheeze.[29,30] Of note was the strong correlation of self-reported background eczema and dermatitis to symptoms of chlorhexidine sensitivity in those with atopy alone or the presence of eczema or dermatitis in the self-reported past history. Plausible explanations for this correlation may relate to a nonimmune-based reaction to chlorhexidine, such as the skin drying effect of both chlorhexidine and frequent hand hygiene, or a direct immune-mediated pathology. In support of nonimmune-mediated causation, the self-reported symptoms of sensitivity to chlorhexidine-based hand hygiene products were increased in staff who reported performing hand hygiene more frequently; however, this correlation would require further validation with control-based studies.

Regarding the possibility that sensitivity symptoms represent an immune-based mechanism, in a study by Andersen et al,[31] 52 (5.4%) of 1,063 eczema patients showed a positive reaction to chlorhexidine gluconate 1% aqueous solution on skin prick testing or 1% petroleum on patch testing. It is not clear whether these patients went on to develop a true allergy to chlorhexidine or were sensitized or what role eczema played in the immune modulation to chlorhexidine in these patients. Given the limited evidence available, it is important that skin prick testing and serum IgE antibodies to chlorhexidine be conducted with a clinical review. A comparison of health care workers with eczema or dermatitis to those with atopy alone or no past history would add further knowledge to this area. Further, a comparison of different types of hand hygiene products and health care worker symptoms should be considered to compare the effects of frequent hand hygiene and skin symptoms. Results from these studies could guide appropriate interventions, which may include avoidance

Table 4
Frequency of self-reported hand hygiene solution use each working day by hospital workers

	n	Not at all	<5	5-10	10-15	15-20	>20
Frequency of hand hygiene solution use per day							
Nursing	143	0	8 (5.6)	11 (7.7)	11 (7.7)	10 (7)	103 (72)
Medical	96	1 (1)	8 (8.3)	14 (14.6)	23 (24)	10 (10.4)	40 (41.7)
Allied health	61	0	13 (21.3)	19 (31.1)	8 (13.1)	7 (11.5)	14 (23)
Clerical	17		11 (64.7)	3 (17.6)	3 (17.6)	0	0
Other	25		7 (28)	3 (4.3)	1 (4)	4 (16)	10 (40)

of chlorhexidine, use of alternative hand hygiene products, or regular skin care with a moisturizer to counteract the drying effects of both chlorhexidine and frequent handwashing on the skin.

Self-reporting of symptoms of sensitivity to chlorhexidine-based hand hygiene products has revealed an impact on a number of health care workers, making this an important occupational health issue. Whether the rates of sensitivity symptoms are increasing because of an immune-based pathology or increasing use of hand hygiene products needs to be elucidated. A clear organizational intervention to prevent symptoms related to this important clinical practice has not been clearly described in the literature and warrants further exploration.

Limitations

The reliance on self-report, overall low response rate, and relatively high prevalence of symptoms suggest a positive reporter bias, as those with symptoms of sensitivity are expected to be more likely to complete the survey than those without. As the participating health services used only chlorhexidine-based hand hygiene products, there was no comparison with other products. However, use of overall staff populations as a denominator suggests the rates of self-reported symptoms of sensitivity to chlorhexidine-based hand hygiene products are similar to previous study populations.

CONCLUSIONS

The development of an occupational chlorhexidine allergy is an important risk to health care workers, particularly nurses. This examination of the prevalence of self-reported symptoms of sensitivity to chlorhexidine hand hygiene solutions among health care workers revealed high reported use and presence of skin symptoms, but there was no correlation with respiratory symptoms. These findings indicate a need for screening programs to identify nurses who develop chlorhexidine sensitivity due to occupational exposure and strategies to mitigate risk through development of alternatives for those with sensitization. Future research should examine the pathogenesis of sensitization of clinical staff to chlorhexidine-based hand hygiene products.

Acknowledgments

We would like to thank Tracy Douglas for her valuable assistance editing the manuscript.

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