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Major article

Effect of chlorhexidine bathing in preventing infections and reducing skin burden and environmental contamination: A review of the literature

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Chlorhexidine bathing is effective in reducing levels of pathogens on skin. In this review, we examine the evidence that chlorhexidine bathing can prevent colonization and infection with health care-associated pathogens and reduce dissemination to the environment and the hands of personnel. The importance of education and monitoring of compliance with bathing procedures is emphasized in order to optimize chlorhexidine bathing in clinical practice.

Patients colonized or infected with health care-associated pathogens often carry the organisms on their skin.[1-3] Such contamination may lead to infection when factors such as devices, catheters, and wounds provide a route for pathogens on skin to reach normally sterile sites. Skin contamination may also contribute to transmission due to environmental shedding and transfer to the hands of personnel.[1-3] Thus, there is a strong rationale for efforts to reduce the burden of pathogens on skin.

During the past decade, a number of studies have examined the use of chlorhexidine bathing as an infection prevention strategy. This review examines the evidence that chlorhexidine bathing can prevent colonization and infection with health care-associated pathogens and reduce dissemination to the environment and the hands of personnel. We also consider recent evidence that chlorhexidine bathing is often suboptimal in clinical practice. The importance of education and monitoring and feedback on compliance with bathing procedures to optimize chlorhexidine bathing is emphasized. The review was not conducted as a systematic review, but the MEDLINE electronic database was searched using broad search terminologies and recent review articles and their references were searched.

CHLORHEXIDINE SPECTRUM OF ACTIVITY AND USE FOR SKIN ANTISEPSIS

Chlorhexidine is a cationic bisbiguanide antiseptic that alters microbial membrane integrity.[4] A variety of formulations are available, with chlorhexidine gluconate being most commonly used in health care settings. Chlorhexidine has broad-spectrum activity against gram-positive and gram-negative bacteria, yeasts, and some lipid-enveloped viruses. Potent sporicidal activity can be induced in chlorhexidine under altered physical and chemical conditions (eg, elevated temperature, altered pH, and addition of ethanol).[5] However, chlorhexidine does not have activity against bacterial spores under the conditions present on skin.

Due to its broad-spectrum antimicrobial activity and excellent safety profile, chlorhexidine is used in a wide variety of disinfectant, antiseptic, and preservative applications.[5] In health care settings, chlorhexidine has been used for several decades for hand hygiene and for disinfection of the skin of patients before surgical procedures and catheter insertion.[4] Chlorhexidine significantly reduces levels of resident and transient skin microbiota and has persistent activity for several hours after application.[6] Chlorhexidine

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occasionally is associated with contact dermatitis, and rarely has been associated with anaphylaxis and hypersensitivity reactions.[4]

EFFECT OF DAILY CHLORHEXIDINE BATHING ON SHEDDING OF PATHOGENS

Skin contamination can be an important source of transmission of health care-associated pathogens through transfer to the hands of personnel and shedding into the environment.[1-3] To test the potential for skin decontamination to reduce transmission, Vernon et al[7] conducted a quasiexperimental study of daily chlorhexidine whole-body bathing in an intensive care unit (ICU). Vancomycin-resistant *Enterococcus* (VRE) was chosen for study as it is often present on the skin of colonized patients and it is a common cause of central line-associated bloodstream infections (CLABSIs). Patients were bathed daily with 2% chlorhexidine cloths during the intervention period and standard soap-and-water baths or cloths cleansing without chlorhexidine was performed during control periods.

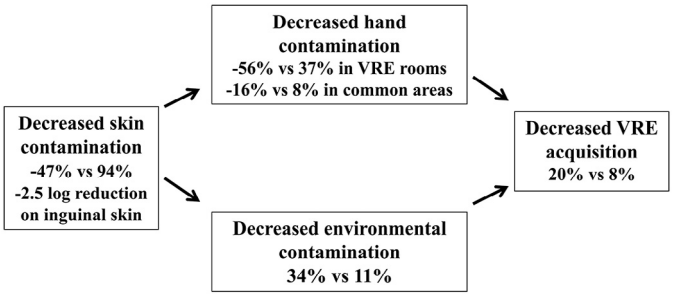

Fig 1. Effect of daily chlorhexidine bathing on skin and environmental contamination and acquisition of vancomycin-resistant enterococci (VRE).

As shown in Figure 1, chlorhexidine bathing was associated with a reduction in detection of VRE on skin. For inguinal skin, there was a 2.5-log reduction in VRE concentrations in the chlorhexidine bathing group that persisted for at least 6-8 hours. The reduction in VRE on skin was associated with significantly reduced VRE contamination in the environment and on the hands of personnel. Moreover, there was a significant reduction in VRE acquisition in the ICU. The findings of Vernon et al[7] provide strong support for the concept of source control as a strategy to reduce dissemination of health care-associated pathogens (ie, reducing the burden of pathogens on the skin as a means to reduce dissemination to the environment or hands). Given its broad spectrum of activity, chlorhexidine bathing represents a horizontal infection prevention approach that can potentially reduce dissemination of multiple pathogens. In addition, it is in theory a very simple and easy to implement intervention because it involves substitution of chlorhexidine bathing for standard soap-and-water bathing.

EFFECT OF DAILY CHLORHEXIDINE BATHING ON COLONIZATION AND INFECTION WITH PATHOGENS

Table 1 provides an overview of 14 studies that have evaluated the effect of chlorhexidine bathing using quasiexperimental, ward-level crossover, or stepped wedge design.[7-22] Several of the studies demonstrated reductions in levels of pathogens, including gram-negative bacilli, on skin.[7,11,18] For example, Popovich et al[18] reported significant reductions in gram-positive and gram-negative bacteria and *Candida* spp on skin. In 12 of the 14 (86%) studies, chlorhexidine bathing was associated with a significant reduction

Table 1
Effect of chlorhexidine gluconate (CHG) bathing on colonization and infection with pathogens

Study	Setting	Chlorhexidine formulation	Design	Outcomes
7	Medical intensive care unit	2% chlorhexidine gluconate (CHG)-impregnated cloths	Quasiexperimental	Decreased vancomycin-resistant enterococci on patients' skin, health care workers' hands, and environment Reduced acquisition of vancomycin-resistant enterococci colonization
11	Medical intensive care unit	4% CHG solution	Quasiexperimental	Decreased *Acinetobacter baumannii* skin colonization and bloodstream infections
10	2 Medical intensive care unit wards	2% CHG-impregnated cloths	2 arm crossover trial	Decreased primary bloodstream infections
6	Medical intensive care unit	2% CHG-impregnated cloths	Quasiexperimental	Decreased central line-associated bloodstream infections and blood culture contamination
12	6 Intensive care units in 4 hospitals	2% CHG-impregnated cloths	Quasiexperimental	Decreased acquisition of methicillin-resistant *Staphylococcus aureus* and vancomycin-resistant enterococci Decreased vancomycin-resistant enterococci bacteremia
17	Long-term acute care hospital	2% CHG solution	Quasiexperimental	Decreased central line-associated bloodstream infection No change in ventilator-associated pneumonia
9	2 Intensive care units	4% CHG solution plus chlorhexidine acetate powder to groin, axilla, and skin folds	Quasiexperimental	Decreased acquisition of methicillin-resistant *S aureus* (non-qacA/B strains)
14	Trauma intensive care unit	2% CHG-impregnated cloths	Quasiexperimental	Decreased methicillin-resistant *S aureus* and *Acinetobacter* spp colonization Decreased central line-associated bloodstream infection
19	Surgical intensive care unit	2% CHG-impregnated cloths	Quasiexperimental	No decrease in central line-associated bloodstream infection
13	Trauma center intensive care unit	2% CHG-impregnated cloths	Quasiexperimental	Decreased central line-associated bloodstream infection
16	4 Medical wards	2% CHG-impregnated cloths	Quasiexperimental	Decreased methicillin-resistant *S aureus* and vancomycin-resistant enterococci infections No change in *Clostridium difficile* infections
21	Hospital-wide	4% CHG solution applied as bed bath or shower daily or 3 times per week	Quasiexperimental	Decreased *C difficile* infections No change in other hospital-associated infections
8	Oncology patients	2% CHG-impregnated cloths	Quasiexperimental	Decreased acquisition of vancomycin-resistant enterococci colonization
15	4 Long-term acute care hospitals	2% CHG-impregnated cloths	Stepped wedge bundle	Decreased *Klebsiella pneumoniae* carbapenemase-producing enterobacteriaceae colonization and infection, all-cause bacteremia, and blood culture contamination

in colonization or infection with 1 or more of the pathogens being studied. Chlorhexidine was associated with beneficial effects when applied using 2% chlorhexidine-impregnated cloths and using cotton cloths with 2% or 4% chlorhexidine solution.

In 1 quasiexperimental study, hospital-wide chlorhexidine patient bathing was associated with a significant reduction in the incidence of health care-associated *Clostridium difficile* infection (CDI), but not in other health care-associated infections.[21] The strength of the observation was increased by the finding of an increase in the incidence of CDI during a washout period in which standard soap-and-water bathing was reinstituted. As noted previously, chlorhexidine does not have sporicidal activity under the conditions present on skin, and therefore the reduction in CDI was unexpected. It was speculated that there may have been an increase in physical removal of spores during the chlorhexidine bathing period or that chlorhexidine might be killing vegetative *C difficile* or inhibiting spore germination on skin. Based on these findings, further studies are needed to examine the effect of chlorhexidine bathing on levels of spores on skin of patients with CDI. However, others have not demonstrated reductions in health care-associated CDI during chlorhexidine bathing.[16]

The 1 quasiexperimental study that did not report a benefit of chlorhexidine bathing was conducted in a surgical ICU.[19] After the switch to chlorhexidine bathing, there was no significant reduction in CLABSIs or other nosocomial infections. It was suggested that the failure to achieve a reduction in CLABSIs might have been related to characteristics of surgical intensive care unit patients. Such patients may have large, open abdominal wounds that may serve as a source of bacteremia that could be misidentified as CLABSIs.

RANDOMIZED TRIALS

Four randomized trials have evaluated the effect of chlorhexidine bathing on hospital-acquired infections.[23-26] Climo et al[24] conducted a multicenter, cluster-randomized, nonblinded crossover trial to evaluate the effect of daily bathing with chlorhexidine-impregnated washcloths on acquisition of multidrug-resistant organisms (MDROs) and the incidence of hospital-acquired bloodstream infections. Nine ICUs and bone marrow transplantation units in 6 hospitals were included. During the chlorhexidine bathing periods, the rates of MDRO acquisition and hospital-acquired bloodstream infection were reduced by 23% and 28%, respectively. Much of the reduction in bloodstream infections was attributable to a reduction in infections with coagulase-negative staphylococci. The benefit of chlorhexidine bathing in reducing bloodstream infections increased with longer length of stay in the unit.

Milstone et al[25] conducted a multicenter, cluster-randomized, crossover trial in critically ill children in 10 ICUs. Bathing was performed using 2% chlorhexidine-impregnated cloths. Chlorhexidine bathing resulted in a statistically significant reduction in bacteremia.

Noto et al[26] conducted a pragmatic cluster-randomized, crossover study in 5 adult intensive care units in a tertiary care medical center. Patients were bathed with 2% chlorhexidine-impregnated cloths or nonantimicrobial cloths (controls). There was no difference between the chlorhexidine and control groups in the primary outcome, which was a composite of nosocomial infections, including CLABSIs, catheter-associated urinary tract infection, ventilator-associated pneumonia, and CDI. In addition, chlorhexidine bathing was not associated with a reduction in secondary outcomes such as hospital-acquired bloodstream infections, blood culture contamination, or clinical cultures yielding MDROs. One criticism of the study design is that the primary end point included infections such as CDI, catheter-associated urinary tract infection, and ventilator-associated pneumonia that would not be expected to be reduced by chlorhexidine bathing. In addition, adherence to chlorhexidine bathing was not monitored.

Boonyasiri et al[23] conducted a randomized, open-label controlled trial in 4 medical ICUs in Thailand. Patients were bathed with 2% chlorhexidine-impregnated cloths or with nonantimicrobial soap. Adherence to bathing procedures was reported to be >95%, but the method of monitoring was not reported. There were no differences in the 5 outcomes, including having all skin sites culture-negative throughout admission or initial positives converted to negative, colonization with MDROs, hospital-acquired infection, length of intensive care and hospital stay, and adverse skin reactions. The authors speculated that the failure to demonstrate a benefit of chlorhexidine bathing in this setting may have been related to the fact that the major colonizing organisms in the ICUs were gram-negative bacilli. Other studies have demonstrated that gram-negative pathogens often have higher minimum-inhibitory concentrations for chlorhexidine than gram-positive pathogens.[27,28] In addition, most of the multidrug-resistant gram-negative bacilli recovered from skin were from the perianal area, suggesting that they may have been shed from the gastrointestinal tract. Chlorhexidine bathing would not be expected to affect gastrointestinal colonization.

IMPORTANCE OF EDUCATION AND MONITORING OF COMPLIANCE

One of the guiding principles of infection prevention is that effective implementation of interventions requires monitoring of compliance of staff with regular feedback on performance. For example, thoroughness of cleaning is often suboptimal and can be significantly improved by monitoring and feedback.[29] However, in published studies, surprisingly little information has been reported on compliance with chlorhexidine bathing procedures. Those studies that have included monitoring have suggested that compliance may often be less than ideal even in the setting of a research study. For example, based on purchasing records, Kassakian et al[16] estimated that compliance with chlorhexidine bathing among general medical patients was 77%. Similarly, Rupp et al[21] estimated compliance based on inventory assessments and found that estimates varied widely by ward, ranging from 45%-95%.

Although in theory chlorhexidine bathing should be easy to implement, 2 recent studies have provided striking demonstrations of the potential for suboptimal implementation of bathing interventions in real-world settings.[17,30] In a long-term acute care hospital, Munoz-Price et al[17] found that constant supervision of staff was essential to ensure that chlorhexidine baths were appropriately given. In the absence of regular evaluations of bathing, staff stopped using chlorhexidine and began bathing patients with baby shampoo. Similarly, in medical and surgical ICUs where daily bathing with chlorhexidine 2% cloths had been implemented 2 years earlier, Supple et al[30] found that none of the patients had detectable chlorhexidine on skin. It was determined that the nursing staff in both intensive care units had abandoned chlorhexidine bathing altogether without the knowledge of the infection control program. As shown in Figure 2, an intervention that included monitoring and feedback on compliance with chlorhexidine bathing was effective in increasing the percentage of skin sites with detectable chlorhexidine to 70%-88%.[30]

The experience of Supple et al[30] suggests that measurement of chlorhexidine on skin may be useful as a means to monitor effectiveness of bathing practices and provide feedback. A simple, rapid colorimetric assay that is commonly used in research studies was used to measure chlorhexidine on skin.[31] The assay is easy to perform and includes reagents that are inexpensive and commercially available.[31] In addition to the improvement in daily intensive care unit bathing, the assay identified deficiencies in preoperative bathing

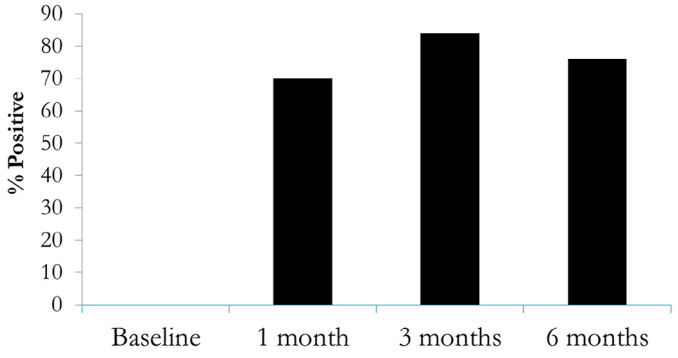

Fig 2. Point-prevalence of medical and surgical intensive care unit patients with detectable chlorhexidine on 1 or more skin sites before and 1, 3, and 6 months after an intervention. Chlorhexidine was measured from 4 skin sites (neck, arm and hand, chest and abdomen, and groin).

that were significantly improved by an intervention. For example, many patients performing preoperative bathing did not have detectable chlorhexidine on their neck because their understanding of the instructions was that they should bathe below the neck. This deficiency was easily corrected through education of nurses and modification of patient education sheets. Similarly, Popovich et al[6] found that patients admitted to ICUs often had low levels of chlorhexidine on their neck and noted that this area received less thorough cleansing when bathing was directly observed. Popovich et al[6] also suggested that measurement of chlorhexidine on skin might be useful as a means to improve bathing performance.

Finally, it should be appreciated that suboptimal application of chlorhexidine may be an issue in real-world settings even if staff and patients are motivated to comply with recommended bathing procedures. In contrast to healthy volunteers and most patients receiving preoperative bathing, patients in ICUs and ill patients on medical wards often have large surgical wounds and numerous lines, catheters, and devices that make it difficult to apply chlorhexidine effectively. These difficulties are akin to the challenges involved in performing effective daily environmental cleaning of a cluttered patient room versus terminal cleaning after patient discharge. In this regard, it is notable that the 1 quasiexperimental study that did not report a benefit of chlorhexidine bathing was conducted in a surgical ICU.[19] The authors noted that many of the patients in the unit had large, open abdominal wounds that could make chlorhexidine application difficult. In addition to providing feedback on compliance, measurement of chlorhexidine on skin in such real-world settings may shed light on some of the challenges involved in providing effective bathing.

CONCLUSIONS

During the past decade, a growing body of evidence has accumulated suggesting that chlorhexidine bathing may be beneficial as a strategy to prevent colonization and infection with health care-associated pathogens. In addition, reduction in skin carriage may reduce dissemination of pathogens to the environment and the hands of personnel. Although reductions in gram-positive pathogens have been reported most frequently, reductions in gram-negative pathogens have also been reported in some but not all studies. Given the evidence that chlorhexidine bathing may be beneficial, this practice is now becoming routine in many facilities, particularly in ICUs. There is evidence that chlorhexidine bathing is not infrequently suboptimal in clinical practice. To optimize bathing in real-world settings, there is a need to develop effective strategies to monitor compliance with bathing protocols and provide feedback to personnel.

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