Reducing the risk of surgical site infections: Does chlorhexidine gluconate provide a risk reduction benefit?

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Chlorhexidine gluconate (CHG) has been available as a topical antiseptic for over 50 years, having broad clinical application throughout the health care environment. Evidence-based clinical studies have shown chlorhexidine gluconate to be a safe and effective perioperative skin-prepping agent. Renewed interest has emerged for use of the antiseptic bath/shower to reduce the microbial skin burden prior to hospital admission. Recent clinical studies have documented that multiple applications of 2% or 4% CHG using a standardized protocol results in high skin surface concentrations sufficient to inhibit/kill skin colonizing flora, including methicillin-resistant Staphylococcus aureus. A new focus for the use of CHG in surgical patients involves irrigation of the wound prior to closure with 0.05% CHG followed by saline rinse. Recent laboratory studies suggest that, following a 1-minute exposure, 0.05% CHG produces a >5-log reduction against selective health care-associated pathogens and reduces microbial adherence to the surface of implantable biomedical devices. General, orthopedic, cardiothoracic, and obstetrical surgical studies have documented the safety of selective CHG formulations in elective surgical procedures. The following discussion will address both the evidence-based literature and preliminary findings suggesting that CHG has a broad and safe range of applications when used as an adjunctive interventional strategy for reducing the risk of postoperative surgical site infections (SSI).

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frequency among selective health care workers (nurses) than the general public. These colonizing staphylococcal isolates had a reduced susceptibility to benzalkonium chloride and CHG compared with gene-negative isolates. Furthermore, it has been suggested that subinhibitory biocide exposure under experimental laboratory conditions will induce qac gene expression. Therefore, there exists a theoretical possibility that exposure to biocides such as CHG could exert a selective pressure on antibiotic-resistant strains, facilitating their survival within the health care environment. However, it is important to note that a “reduced susceptibility” to CHG does not necessarily translate into diminished antimicrobial effectiveness when the biocide is used at the appropriate (application) concentration. Further surveillance studies are warranted, documenting future changes in the antiseptic activity of CHG against clinically relevant microbial populations.

MAKING THE CLINICAL CASE FOR CHG IN THE SURGICAL PATIENT POPULATION

Preadmission skin antisepsis

The concept of the preadmission shower as a risk reduction strategy was addressed in the 1999 Centers for Disease Control and Prevention Hospital Infection Control Practices Advisory Committee document, Guideline for the Prevention of Surgical Site Infection. A preoperative antiseptic shower or bath decreases skin microbial colony counts. In a study of >700 patients who received two preoperative antiseptic showers, chlorhexidine reduced bacterial colony counts nine-fold (2.3 × 10² to 0.3), while povidone-iodine or triclocarban-mediated soap reduced colony counts by 1.3- and 1.9-fold, respectively.”

This process was designated by the Centers for Disease Control and Prevention guidelines as a category 1B clinical practice and is “strongly recommended.” Whereas there is universal agreement that a 2% or 4% CHG whole-body bath or shower will reduce bacterial colonization of the skin, there was no definitive data to suggest that this practice was an effective strategy for reducing postoperative surgical site infections. The Cochrane Collaborative review published in 2007 reviewed 9 clinical trials from 1983 to 2005 and suggested that existing evidence-based data did not justify continuation of this practice. A recent meta-analysis evaluated 16 clinical trials from 1979 to 2011, involving a total of 9,980 patients, came to a similar conclusion that whole-body showering or cleansing showed no benefit in preventing postoperative surgical site infection. A separate analysis published in 2011 found that many of the previous clinical studies were technically and scientifically flawed and that a rigorous standardization was lacking. Whereas most analyses appear not to support the routine use of the preadmission whole-body cleansing or showering, several factors should be considered when evaluating this low risk and low cost intervention:

- CHG surface skin concentrations accumulate with repetitive application, and, therefore, single application may not approach concentrations sufficient to inhibit skin flora.
- Standardization is an important component of any antiseptic body cleansing or showering process; previous studies have failed to validate this aspect of the practice.
- A discussion of measuring patient compliance is often excluded from most published protocols.

In an effort to address the impact of protocol standardization and repetitive application on skin surface concentrations of CHG, a randomized, prospective study was conducted in the Department of Surgery at the Medical College of Wisconsin comparing the application of 4% CHG aqueous soap to 2% CHG-impregnated polyester cloths. Several variables were considered: (1) number of applications, (2) timing of the applications, (3) CHG application at multiple body sites, and (4) specific application instructions provided to the participants (patients). Volunteers were randomized into 3 groups: (1) showering or cleansing once in the evening; (2) showering or cleansing once in the morning; and (3) showering or cleansing twice, in the evening and morning. In an exploratory pilot study, individuals were given 4% CHG without any specific instructions except they were told to shower once in the evening, once in the morning, or twice (evening and morning). In this nonstandardized process, the skin surface concentrations of CHG as measured at 5 separate anatomic sites were often below the MIC₉₀ concentration require to inhibit or kill staphylococcal skin isolates. However, when specific and detailed timed application instructions (standardized) were provided to the volunteers (patients), even a single shower (4%) or cleansing (2%) resulted in CHG skin surface concentrations well above that required to inhibit or kill staphylococcal microbial populations. The highest skin surface concentrations were observed when 2 showers or cleansings were implemented. The ratio of C₉₀/MIC₉₀ ranged from 25.3 for the 4% formulation to 349.1 for the 2% CHG-impregnated cloths.

Several recent reports using a standardized process have documented the benefit of preadmission skin antisepsis. In an orthopedic population undergoing total joint replacement, the preinterventional infection rate was 3.19% (N = 727), whereas, in a postinterventional population where patients were instructed to cleanse the night before and once again in the hospital ambulatory area prior to surgery using the 2% CHG-impregnated cloths, the infections rate was 1.59% (N = 424). A second study (quality initiative) in total hip and knee replacement, gastric bypass, C-section, and bone fusion patients (N = 5,570), using a bundled approach of a standardized active methicillin-resistant Staphylococcus aureus (MRSA) surveillance and presurgical antisepsis protocol (application of 2% CHG-impregnated wipes, once prior to surgery), documented a significant reduction (P < .019) in surgical site infection postimplementation (0.57%, N = 71,225) compared with the preinterventional period (1.55%, N = 17,1094). A third study in an orthopedic patients population using a bundling strategy of active surveillance for methicillin-susceptible Staphylococcus aureus/MRSA, decolonization in all positive patients (nasal mupirocin, twice daily for 5 days), and total body wash with 4% CHG aqueous (5 days) found a significant reduction in the rate of selective MRSA infections (P <.032) and total surgical site infections (SSI) (P < .0093) during the intervention period (N = 7,019) compared with a control period (N = 5,293).

An unresolved question regarding the preadmission application of CHG is what is the optimal number of applications prior to surgery? Because skin surface activity is enhanced following multiple applications of CHG, most practitioners are recommending 2 to 5 separate application prior to surgery. Each patient undergoing an elective surgical procedure at Froedtert Hospital in Milwaukee, Wisconsin, is given an instruction sheet (Fig 1) describing the preadmission body cleansing process using a 2% CHG-impregnated polyester cloth. Those instructions recommend a minimum of 2 applications prior to admission (night before and morning of surgery). This information is also conveyed orally to the patient when she or he undergoes preoperative testing. The instructional sheet serves as a reinforcement and point of reference for the patient. Compliance is of course a significant component of any successful patient-directed interventional strategy. A recent study conducted in an orthopedic patient population undergoing total joint or spine surgery looked at compliance rates for preoperative use of CHG total body washing and intranasal mupirocin.
administration. Patients were required to purchase out-of-pocket both the CHG aqueous body wash and topical mupirocin from a local pharmacy. A total of 81% of patients followed the nasal decolonization regimen, and 89% followed the CHG body-washing regimen. Although patient compliance was viewed as relatively high, one barrier to compliance was ease of obtaining CHG and mupirocin, which was viewed as difficult by some patients.25 Ideally, both CHG and, in the case of the decolonization regimen, mupirocin should be provided to the patient along with printed instructions in an effort to maximize the benefit and enhance compliance to the interventional bundle.

Current evidence-based studies would suggest that preadmission skin surface cleansing with CHG-impregnated polyester cloths or application of CHG to the skin as an aqueous solution would appear to have equal efficacy.22-24 Similar findings have been noted in patients undergoing daily bathing/cleansing in the intensive care unit. A recent meta-analysis has documented that bathing with aqueous CHG or skin surface cleansing with CHG-impregnated cloths were equally effective (P = .03, P < .006, respectively) in reducing the incidences of health care-associated bloodstream infections.

CHG in perioperative skin antisepsis

Skin antisepsis is viewed as a fundamental component of the perioperative effort to reduce the risk of surgical site infections, and several antiseptic agents have been identified as beneficial to this process.16 The iodophors, CHG, or an alcohol-containing derivative of both products are the most common agents used in surgery. Both the iodophors and chlorhexidine exhibit a broad spectrum of antimicrobial activity, but, as previous discussed, CHG demonstrates an accumulative or residual activity on the skin, and its activity does not appear to be influenced by blood or tissue proteins.7 Does CHG offer a selective advantage as a skin-prepping agent for reducing the risk of surgical site infections? Most studies looking at CHG efficacy have focused on what would be viewed as “surrogate” studies, where SSI reducing is not the primary outcome but rather reduction of skin surface flora at the incision site. A study conducted in patients undergoing foot surgery was randomized to 1 of 3 skin-prepping groups; 3% parachlorometaxylenol (PCMX), 0.7% iodine + 74% isopropyl alcohol, or 2% CHG + 70% isopropyl alcohol. The study found that the CHG/alcohol combination resulted in a significant (P < .001) qualitative and quantitative reduction in foot flora (hallux and toes sites) compared with study comparators.26 A second study compared 2% CHG + 70% isopropyl alcohol to 0.7% iodine + 74% isopropyl alcohol or 0.75% iodine scrub + 1% iodine paint in patients undergoing elective shoulder surgery. The authors found that the CHG/alcohol skin-prepping solution was superior to the other 2 agents (P < .01) in reducing staphylococcal skin surface flora from the incision site.27 In a randomized clinical trial in patients undergoing vaginal hysterectomy (N = 50), the authors found that patients who were prepped with 4% CHG compared with 10% povidone-iodine demonstrated at 30 minutes a significant (P < .002) reduction in contaminating skin flora compared with the iodophor group.28 This statistical benefit, however, did not persist at 90 minutes postapplication. A “surrogate” study published in 2012 compared the efficacy of 0.7% iodine + 74% isopropyl alcohol against 2% CHG + 70% alcohol in patients undergoing lumbar spine surgery. Both agents were equally effective in eradicating (quantitatively) flora overlying the lumbar spine.29
Surrogate studies, although helpful in delineating microbiologic efficacy, do not supplant the benefits of a rigorous clinical trial in assessing clinical efficacy. However, few studies have adequately assessed the comparative clinical advantage of one skin-prepping agent over another in a prospective, randomized clinical trial. At the University of Virginia, surgical investigators conducted a single institution, quasiexperimental study in general surgical patients ($N = 3,209$ operations) looking at clinical outcomes associated with 3 separate skin-prepping regimens using a sequential (6 month) implementation design: (regimen A) 10% povidone-iodine scrub combination with an isopropyl alcohol application between steps; (regimen B) 2% CHG + 70% isopropyl alcohol; and (regimen C) 0.7% iodine povacrylex + 74% isopropyl alcohol. Patients were followed for 30 days postoperatively as part of an ongoing American College of Surgeons National Quality Improvement Program initiative. The primary outcome was overall rate of SSIs by 6 months performed in an intent-to-treat manner. The results were highly provocative with the lowest infection rate observed in regimen C, 3.9%, compared with 7.1% for regimen B ($P < .002$). Subgroup analysis documented no difference in outcomes between patients prepped with povidone-iodine scrub paint or prepped with iodine povacrylex in isopropyl alcohol; these patients had significantly lower surgical site infection rate compared with patients prepped in the 2% CHG and 70% isopropyl alcohol (4.8% vs 8.2%, respectively; $P < .001$) group. In a separate multicenter, prospective, randomized clinical trial comparing 10% povidone-iodine ($N = 409$) with 2% CHG + 70% isopropyl alcohol ($N = 440$) in clean-contaminated surgical cases, investigators found that the overall rate of SSI was significantly lower in the CHG/iodine group compared with povidone-iodine group (9.5% vs 16.1%, respectively, $P < .004$). The CHG/iodine combination was superior to the povidone-iodine group in reducing the risk of both superficial incisional (4.2% vs 8.6%, respectively, $P < .008$) and deep incisional (1% vs 3%, respectively, $P = .05$) surgical site infections. Whereas these 2 clinical trials present conflicting results, from an evidence-based perspective, the latter (Darouiche et al's study) is viewed as methodologically superior. However, it should be pointed out that the Darouiche et al study is also perceived as flawed because the CHG/iodine skin-prepping agent was not compared against an alcohol/iodine comparator. It should, however, be noted that this study is the first clinical trial to document the benefit of a selective skin-prepping agent (2% CHG/70% isopropyl alcohol) to significantly reduce the risk of superficial and/or deep incisional surgical site infections in clean-contaminated surgical procedures.

In 2010, a meta-analysis of 7 randomized clinical trials ($N = 3,614$ patients) was published comparing CHG (0.5%-4%) with iodine (0.7%-10%) for preoperative skin antisepsis as an effective risk reduction strategy for preventing surgical site infections. The analysis noted that use of CHG was associated with fewer surgical site infections (adjusted risk ratio, 0.64; 95% confidence interval: 0.51-0.80) compared with iodine. In a cost benefit model, sensitivity analysis documented that switching from iodine to CHG resulted in a net savings per surgical case of $16 to $24, projecting a yearly saving of $349,904 to $568,594 per year for the collective surgical services. The myriad of “surrogate” and clinical studies suggest that CHG + alcohol combination would appear to be the most effect skin antiseptic agent for reducing the risk of surgical site infections. The addition of an alcohol base lends an enhanced component to the broad-spectrum activity of CHG, further augmented by documented residual activity of CHG on the surface of the skin. One cautionary comment: any skin antiseptic agent containing alcohol, including CHG must be allowed to dry prior to draping so as to reduce the likelihood of a fire occurring during electrocautery.

**Intraoperative irrigation: Does CHG have a role in reducing risk?**

The view that “the solution to pollution is dilution” has been the driving force behind the widespread application of intraoperative irrigation across the spectrum of surgical services. The combination of saline irrigation and debridement plays a major role in the management of traumatic open fractures in orthopedic surgery. Intraoperative (saline) lavage has been a long-standing tradition in general surgery, especially following spillage of fecal contents after penetrating trauma or intraoperative injury. However, the addition of antimicrobial agents to the intraoperative lavage fluid has been viewed within selective surgical disciplines as an important strategy for reducing postoperative infection. Unfortunately, in an era of evidence-based medicine, it is difficult to assess the clinical efficacy in light of the paucity of well-designed randomized, controlled clinical trials. Therefore, in the absence of established clinical guidelines, the scientific merit of this practice remains purely within the realm of dogmatism.

The process of augmenting irrigation fluids with additives such as antimicrobials has been a continuous source of controversy in surgery. An experimental study published in 1990 noted that, following penetrating bowel injury, there is a rapid contamination of the serosal mesothelium by both gram-positive and gram-negative fecal populations, stimulating an intense inflammatory response (Fig 2A). A copious saline lavage was highly effective (5- to 6-log reduction) at removing “free particulate” contamination from the peritoneal cavity. However, peritoneal lavage, even with the addition of selective antibiotics (cephazolin, kanamycin, and/or metronidazole), was ineffective at reducing peritoneal mesothelial contamination. Mechanistically, most antimicrobials agents are effective against microorganisms when drug exposure occurs during their logarithmic growth phase. Therefore, the process of antibiotic-lavage or irrigation does not realistically afford sufficient contact time to efficiently kill or inhibit bacterial growth within the peritoneal cavity. In addition to the question of clinical efficacy, selective case reports have suggested that local antimicrobial irrigation may be associated with severe intraoperative anaphylaxis, which has been seen with bacitracin irrigation during selective surgical procedures (cardiac, orthopedic, general, and neurosurgical). In a study published in 2003, investigators attempted to retrospectively evaluate the benefits of antibiotic (neomycin/bacitracin) irrigation versus normal saline following pacemaker insertion ($N = 418$), coronary artery bypass procedures ($N = 1,464$), and laminectomy ($N = 941$). A total of 2,823 surgical procedures was evaluated: 1,043 irrigated with an antibiotic, and 1,780 used normal saline. There was no significant difference in the surgical wound infection rate between those patients irrigated with antibiotic solution versus normal saline. A retrospective analysis of 176 consecutive appendectomy cases found that intraoperative saline irrigation in open versus laparoscopic appendectomy did not prevent intra-abdominal abscess formation. A recent retrospective study involving 1,063 surgical appendectomy cases suggested that abdominal irrigation with an imipenem ($N = 194$) solution was superior ($P < .05$) to irrigation with normal saline ($N = 661$) or Dakin’s solution ($N = 208$) in cases of appendicitis. However, the breakdown of parenteral administration of antibiotics per irrigation group was not disclosed in this paper, therefore making it difficult to assess the actual efficacy of the antimicrobial irrigation solution. Some recent papers in the orthopedic literature suggest that, even in selective contaminated (infected) cases, antibiotic irrigation is unlikely to have a significant impact on improving clinical outcome.

Several studies have suggested a benefit of using antiseptic solutions to irrigate the surgical wound. The most common agent for irrigation is povidone-iodine, which is active against a broad
Implantation of polypropylene mesh for repair of large ventral abdominal defect. The serosal mesothelium during fecal peritonitis and host inflammatory response to contamination (magnification, ×6,000).

Assessing microbial survival on selective biomedical device surfaces following exposure to 0.05% CHG antiseptic solution (Table 2). Exposure to a concentration of 0.05% CHG effectively produced a 5- to 6-log reduction in microbial recovery at 1 and 5 minutes, respectively (Table 1). This effective log reduction was observed with both gram-positive and gram-negative surgical isolates, including a biofilm-forming strain recovered from a prosthetic device-related infection. Intraoperative irrigation using a safe and effective biocide, especially prior to wound closure, could offer a mechanistic advantage over traditional antibiotic irrigation, which requires a substantially longer period of exposure to the surgical wound. Device implantation has become a common procedure in all surgical services, and, in the case of repair of an abdominal defect with mesh, the open wound can be quite large (Fig 2B), exposing both the tissues and implant to risk of environmental contamination.

Table 1 Log reduction of selective gram-positive and gram-negative surgical isolates following timed exposure to 0.05% chlorhexidine gluconate solution

<table>
<thead>
<tr>
<th>Organism</th>
<th>CFU</th>
<th>60 Seconds</th>
<th>5 Minutes</th>
</tr>
</thead>
<tbody>
<tr>
<td>MSSA</td>
<td>8.7</td>
<td>3.4 (=5 logs)</td>
<td>2.6 (=6 logs)</td>
</tr>
<tr>
<td>MRSA</td>
<td>8.4</td>
<td>3.5 (=5 logs)</td>
<td>2.6 (=6 logs)</td>
</tr>
<tr>
<td>Staphylococcus epidermidis&lt;sup&gt;+&lt;/sup&gt;</td>
<td>8.3</td>
<td>2.9 (=5 logs)</td>
<td>2.5 (=6 logs)</td>
</tr>
<tr>
<td>Escherichia coli&lt;sup&gt;+&lt;/sup&gt;</td>
<td>8.8</td>
<td>2.7 (=6 logs)</td>
<td>2.1 (=6 logs)</td>
</tr>
<tr>
<td>Escherichia aerogenes&lt;sup&gt;+&lt;/sup&gt;</td>
<td>8.9</td>
<td>3.1 (=5 logs)</td>
<td>2.8 (=6 logs)</td>
</tr>
</tbody>
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CHG, Colon-forming units; MRSA, methicillin-resistant Staphylococcus aureus; MSSA, methicillin-susceptible Staphylococcus aureus.


Biofilm-producing strain from vascular graft infection.

In a recent series of in vitro pilot studies (unpublished data), we assessed the antiseptic efficacy of 0.05% CHG: (1) by using time-kill kinetics against selective surgical isolates (Table 1) and (2) by assessing microbial survival on selective biomedical device surfaces following exposure to 0.05% CHG antiseptic solution (Table 2). Exposure to a concentration of 0.05% CHG effectively produced a 5- to 6-log reduction in microbial recovery at 1 and 5 minutes, respectively (Table 1). This effective log reduction was observed with both gram-positive and gram-negative surgical isolates, including a biofilm-forming strain recovered from a prosthetic device-related infection. Intraoperative irrigation using a safe and effective biocide, especially prior to wound closure, could offer a mechanistic advantage over traditional antibiotic irrigation, which requires a substantially longer period of exposure to the surgical wound. Device implantation has become a common procedure in all surgical services, and, in the case of repair of an abdominal defect with mesh, the open wound can be quite large (Fig 2B), exposing both the tissues and implant to risk of environmental contamination.

Table 2 documents the reduction in mean microbial recovery of 3 selective surgical isolates from the surface of 4 separate inert biomedical surfaces. Following a 60-second exposure to 0.05% CHG, there was a significant reduction (P values ranging from < .05 to < .01) in microbial recovery from the surface of both vascular and abdominal implantable devices. Previous studies have demonstrated that implant devices are highly susceptible to wound contamination, leading to occult infection often presenting weeks or months postoperatively. When a device such as a prosthetic vascular graft is contaminated during insertion, the contaminating flora will down-regulate its metabolism, multiplying slowly on the surface of the device until reaching a critical density at which time the host recognizes that an infectious process is occurring. Irrigating the surgical wound and surface of an implantable device with 0.05% CHG prior to wound closure would likely be an effective and safe risk reduction strategy, a logical alternative to the questionable practice of antibiotic irrigation (lavage). Further clinical studies are warranted to validate the benefit of this potential intervention strategy.

Final consideration: Safety of CHG in the surgical patient population

The incidence of skin hypersensitivity associated with use of CHG has been reported to be rare. Preadmission whole-body cleansing and perioperative skin prepping with 2% or 4% CHG has been documented to be safe and effective risk reduction strategy for preventing surgical site infection. Selected animal models have documented meningeal toxicity following direct application of CHG into neural tissues. In actual clinical practice however, when CHG is allowed to thoroughly dry, it been shown to be a safe, efficacious skin disinfectant and can be used for epidural access and cranial or spinal neurosurgical procedures. Vaginal application of CHG in concentrations ranging from 0.05% to 1% has...
been shown to be safe with minimal adverse events. Results of a randomized trial comparing 10% povidone-iodine with 4% CHG for vaginal hysterectomy found CHG to be as safe as povidone-iodine for vaginal tissues. However, care should be taken when applying CHG to avoid contact with the middle ear or areas adjacent to the eyes. At Froedtert Hospital, patients who shower or cleanse with CHG prior to admission are instructed to avoid getting CHG in the eyes or external ear canal and to immediately rinse if they experience any burning or itching sensation following application.

Is CHG bathing or cleansing an appropriate risk reduction strategy for young children or infants? In adults, CHG is poorly absorbed through intact skin, whereas, in infants and young adults (3 months to 17 years), investigators have detected trace amounts of CHG in blood following skin surface cleansing. However, no evidence was found suggesting that repeat exposure to CHG was associated with systemic accumulation or adverse events. The strength of topical CHG concentration does appear to influence detectable levels in the blood: 1% CHG solutions yielded higher blood level than 0.25% or 0.5%. A recent survey of 100 neonatal intensive care units across the United States found that CHG is being used safely in young infants, CHG is currently not recommended (Food and Drug Administration) for use in infants <2 months of age. The antiseptic benefits of CHG are fully documented; however, further studies are warranted to assess the safety and efficacy of CHG preadmission bathing/cleansing in young infants, especially infants less than 2 months of age.

**References**


