

Evidence Summary: Wound management – Chlorhexidine

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QUESTION

What is the best available evidence regarding use of chlorhexidine in wound cleansing?

A review of the evidence on use of chlorhexidine in wound care indicates that research on its effectiveness in reducing bacterial burden is limited to preparations of 1% or less concentration and has primarily been conducted in laboratory settings. While effectiveness in eradicating bacteria has been tested in-vitro and animal studies, the limited research in clinical settings fails to demonstrate an associated improvement in the rate of wound healing. Histological findings indicate toxicity of chlorhexidine to proliferating skin.^{1, 2, 3} There is no strong clinical evidence that chlorhexidine significantly impedes wound healing; however, selection of alternative antiseptics [e.g. polyhexamethylene biguanide (PHMB)] appropriate to the clinical context should be considered. Evaluation of research findings should be viewed with consideration to the appropriateness of concentration of chlorhexidine preparations being used.

CLINICAL BOTTOM LINE

Chlorhexidine preparations

Chlorhexidine is available for two primary purposes:¹

- Chlorhexidine in a 0.05% dilution is designed for wound cleansing, on which this evidence summary focuses.
- Chlorhexidine in a 2% and 4% dilution is designed for surgical skin preparation and as a hand scrub. (See Related Evidence Summaries section)

Microbiology

Chlorhexidine, a biguanide, is a broad spectrum anti-bacterial that inactivates gram positive and negative bacteria through penetration of outer and inner cell membranes.² It has an affinity for binding to skin and mucous membranes.⁴ However, its antiviral activity is variable, mycobacteria are resistant to it and it has no effect on spores.⁵ (Level 5c)

It is commonly used in combination with gluconic acid — chlorhexidine gluconate (CHG). Bactericidal activity of CHG increases as the concentration increases.⁵ A controlled in-vitro study⁶ demonstrated that a wide range of bacteria were susceptible to CHG at concentrations up to 1%. *Escherichia Coli* and *Salmonella spp.* were most susceptible to CHG, with 100% bacterial inhibition at concentrations below 0.01%. (Level 5c)

An in-vitro study of the efficacy of 0.05% CHG on five organisms including methicillin-resistant *Staphylococcus aureus* (MRSA), methicillin-susceptible *S. aureus* (MSSA), *E.coli* and *E. aerogenes*, produced a 5–6 log reduction in microbial recovery at one and five minutes.⁷ Based on these

results, the authors suggested that irrigating a surgical wound and surface of an implantable device with 0.05% CHG for 1 minute followed by a saline rinse was likely to be an effective and safe alternative to antibiotic irrigation. (7) (Level 5c) Chlorhexidine gluconate (with sterile water) is currently the only antiseptic with US Food and Drug Administration (FDA) clearance to use as an irrigating fluid in a medical device.⁸

Four studies^{9, 10, 11, 12} (Level 5c) compared the effectiveness of chlorhexidine acetate 0.5% (CA) with other topical antiseptic dressings in full-thickness rat burn wounds. In *Acinetobacter baumannii* — contaminated burns¹¹ CA prevented the penetration and systematic spreading of the bacteria. However, neither CA nor silver sulphadiazine were as effective as a nanocrystalline silver dressing in removing the bacteria from the eschar ($p < 0.001$ and $p < 0.05$) respectively. A second study¹⁰ examined the effect of chlorhexidine acetate 0.05%, nanocrystalline silver and fusidic acid 2% on MRSA. Both the nanocrystalline dressing and CA prevented the systemic spread of MRSA but the CA did not prevent deep muscle invasion by the MRSA. The fusidic acid 2% had the added effect of removing the MRSA from the eschar, which in this study the nanocrystalline silver dressing did not.

A third study¹² tested the effectiveness of four topical antiseptics against multi-drug resistant *Pseudomonas aeruginosa*. Only two of the antiseptic dressings — nanocrystalline silver coated and silver sulphadiazine 1% dressings — were effective ($p < 0.05$), while the results for chlorhexidine acetate and citric acid were not significant. The fourth study⁹ compared the topical antifungal effect of nanocrystalline, silver, chlorhexidine 0.05% and nystatin on *Candida albicans* contaminated burns. Although the results for both the silver and nystatin compared to the control group (no topical agent applied) were statistically significant (both $p < 0.001$), the mean eschar concentrations were not significantly different between the CA and control groups and CA only prevented the penetration and spreading of the fungus in half the rats.

Studies of antimicrobial properties of chlorhexidine in the clinical wound care setting are lacking. Its action is pH dependent within a range of that includes wound surfaces.⁵ (Level 5c) However, expert opinion proposes that body fluids and tap water inactivate chlorhexidine's antibacterial properties.¹ (Level 5b)

Histological findings

Data from an in-vitro study³ found that chlorhexidine was cytotoxic to human dermal fibroblasts at concentrations of 5–2400 times below those used in clinical practice. (Level 5c) Evidence from in-vitro studies suggests that fibroblasts and keratinocytes exposed to 0.05% chlorhexidine for 15 minutes are non-viable within 24 hours.¹ (Level 5c) Another in-vitro study found that after 96 hours of exposure to chlorhexidine at

a concentration of 0.0032% there was a significant reduction in fibroblast proliferation ($p=0.05$). However, chlorhexidine at a concentration of 0.0004% was associated with a significant increase in fibroblast proliferation ($16\% \pm 7\%$, $p=0.05$).¹³ (Level 5c)

One histological study ($n=17$) showed that after six weeks of treatment with 5% CHG, chronic leg ulcers exhibited a decrease in microvessels, neutrophils, fibroblasts and dendrocytes compared to ulcers treated with normal saline.¹⁴ (Level 1d) Expert opinion suggested that the decrease in microvessels might not be a significant issue as there was an excessive increase in vasculature related to lipodermatosclerosis in the ulcer bed, i.e. although some microvessels may not survive exposure to 5% CHG, this only reduces microvessels from a pathogenically high level to a 'normal' level.¹⁴ (Level 5b)

The effect of chlorhexidine on human articular cartilage has been of particular concern, with a number of cases of marked chondrolysis and subsequent joint damage being reported. An in-vitro study demonstrated that exposure of non-arthritic human cartilage to chlorhexidine for one minute reduced cell metabolic activity by 14%, which was not significant, but exposure for one hour had a marked effect — 86% reduction ($p<0.001$). In arthritic cartilage even exposure of one minute had a significant impact on metabolic activity (43% reduction, $p<0.05\%$).¹⁵ (Level 5c)

Effectiveness in promoting healing

In one split-body RCT ($n=24$) 12.5% of patients receiving treatment with chlorhexidine diphosphanilate (CHP) cream at concentrations from 0.25% to 1% were assessed as having delayed wound healing (decreased epithelialisation) in leg ulcers.¹⁶ (Level 1c)

One split-body RCT with no blinding ($n=17$) found no significant difference in time to complete healing between chronic leg ulcers treated with 5% CHG compared to those treated with normal saline (14 weeks, 95% CI 7 to 17 versus 15 weeks, 95% CI 7 to 19).¹⁴ (Level 1d) (Note: chlorhexidine at concentrations of 5% is generally not considered to be a wound care product.¹ In the same study an indirect comparison between groups ($n=34$) provided evidence that povidone iodine 10% was associated with superior wound healing outcomes compared to 5% CHG after six weeks of treatment [median of 11 weeks to complete healing (range 9–17 weeks) versus median of 14 weeks (range 7–17 weeks)].¹⁴ (Level 1d)

Effectiveness in managing pain

One split-body RCT ($n=24$) found no statistically significant difference in pain levels up to 120 minutes following application of CHP cream (0.25% to 1% concentrations) to partial thickness burns compared to 1% silver sulphadiazine or the emollient vehicle alone. Pain ratings were lower for concentrations of CHP less than 0.5% compared with 1% CHP.¹⁶ (Level 1c)

Contraindications and side effects

- Chlorhexidine is reported to be associated with low levels of skin irritation and is generally well tolerated when used at appropriate concentrations. It is also considered to be a weak allergen but there have been reported cases of allergic contact dermatitis, urticaria and anaphylactic reactions^{17, 18} (Level 4c)

- Do not apply to areas adjacent to the eyes⁷ (Level 4c)
- In one RCT, severe pain associated with 2% CHP led to early cessation of its use to manage partial thickness burns. The response appears to be related to the higher CHP concentration.¹⁶ (Level 1c)
- CGH is not recommended for use in infants < 2 months of age.⁷

OTHER FACTORS FOR CONSIDERATION

Care staff rated CHP cream difficult to remove from partial thickness burns.¹⁶ (Level 1c)

CHARACTERISTICS OF THE EVIDENCE

This evidence summary is based on a structured literature and database search including ten relevant third world health care journals combining search terms that describe wound management and chlorhexidine. The evidence in this summary comes from:

- One small split-body RCT in which double blinding was reported¹⁶ (Level 1c)
- One non-blinded split-body RCT¹⁴ (Level 1d)
- One case series¹⁸ (Level 4c)
- Five in-vivo laboratory studies^{7, 9, 10, 11, 12} (Level 5c)
- Four in-vitro studies^{3, 6, 13, 15} (Level 5c)
- Six literature reviews^{1, 2, 4, 5, 8, 17} (included various levels of evidence)

BEST PRACTICE RECOMMENDATIONS

There is insufficient evidence on the safety of and effectiveness of chlorhexidine in reducing bio-burden and promoting wound healing in concentrations designed for wound care (i.e. 0.05% or more dilute) to make a recommendation on its use as a wound care product.

RELATED EVIDENCE SUMMARIES

JB1 11600 Community-associated methicillin-resistant *Staphylococcus Aureus*: Chlorhexidine Gluconate body washing.

JB1 11073 Surgical site infections: Intensive care and Chlorhexidine Gluconate bathing.

JB1 9253 Multidrug resistant organisms: Chlorhexidine Gluconate bathing

JB1 9254 Surgical site infections: Chlorhexidine Gluconate bathing

JB1 9364 Bloodstream infections (Paediatrics): Chlorhexidine Gluconate bathing

JB1 9252 Central-line associated bloodstream infections: Chlorhexidine Gluconate bathing

JB1 864 Surgical wound infections (postoperative): Pre-operative skin antiseptics.

JB1 468 Newborn umbilical cord care

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