American Journal of Infection Control 45 (2017) 180-9

Contents lists available at ScienceDirect

American Journal of Infection Control

journal homepage: www.ajicjournal.org

State of the Science Review

Skin antisepsis with chlorhexidine versus iodine for the prevention of surgical site infection: A systematic review and meta-analysis

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Key Words:
Surgical site infections
Preoperative antisepsis
Health care–associated infections
Chlorhexidine
Iodine

Background: Surgical site infection (SSI) is one of the most frequent health care–associated infections. One of the practices to reduce their incidence is preoperative skin antisepsis. Two of the most commonly active components used are chlorhexidine gluconate and povidone iodine. Of 3 reviews conducted between 2010 and 2012 comparing antiseptics, 2 were in favor of chlorhexidine; however, the latest was unable to draw conclusions.

Purpose: To verify whether recent evidence supports the hypothesis that chlorhexidine in preoperative antisepsis is more efficient than other antiseptics in reducing SSI rates.

Procedures: We conducted a systematic review from 2000-2014 in all languages. The primary end point was SSI incidence and secondary skin bacterial colonization.

Results: Nineteen studies were included. Meta-analysis were conducted for comparable studies for both outcomes. The results of the meta-analysis, including all of the studies in which chlorhexidine was compared with iodophor, were in favor of chlorhexidine for both SSI incidence (risk ratio [RR], 0.70; 95% confidence interval [CI], 0.52-0.92) and bacterial skin colonization (RR, 0.45; 95% CI, 0.36-0.55).

Conclusions: There is moderate-quality evidence supporting the use of chlorhexidine for preoperative skin antisepsis and high-quality evidence that the use of chlorhexidine is associated with fewer positive skin cultures. Further rigorous trials will be welcomed to attain stronger evidence as to the best antiseptic to be used before surgery.

Surgical site infections (SSIs) are one of the most frequent health care–associated infections (HCAIs), accounting for approximately 20% of all HCAIs and approximately 38% of the HCAIs in surgical patients. They have an incidence of up to 19%, depending on the kind of surgery.[1-3]

SSIs may involve the superficial or deep layers of the incision (two-thirds) or the organ or space manipulated or traumatized (one-third).[4]

SSIs can range from a wound discharge to a life-threatening condition, and they are associated with considerable morbidity. SSIs lead to an increase in the length of hospital stay from 3.3-32.5 days, and patients are twice as likely to die, twice as likely to spend time in

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Funding/support: A.L.C. reports receiving a research grant from CareFusion Italy.
Conflicts of interest: None to report.

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http://dx.doi.org/10.1016/j.ajic.2016.09.017

intensive care, and 5 times more likely to be readmitted after discharge.[5-10]

Health care costs increase substantially for patients with SSI. In the United States, approximately 500,000 SSIs occur each year, with 3.7 million excess hospital days and >$1.6 billion in excess hospital costs per year.[11] In the United Kingdom, the excess cost for each infection has been calculated from £959-£6,103.[10] In the European Union, SSIs exact an economic toll of €1.5-€19.1 billion per year.[12]

The main additional costs are related to reoperation, extra nursing care, and drug treatment and litigation.

SSI prevention

Practices to prevent SSI are aimed at minimizing the number of microorganisms introduced into the operative site or enhancing the patient's defenses against infection by, for example, removing microorganisms that normally colonize the skin; preventing the multiplication of microorganisms at the operative site (eg, by using prophylactic antimicrobial therapy); minimizing tissue damage; and preventing access of microorganisms postoperatively using a wound dressing.[13]

The removal of transient bacteria and reduction of the number of commensal organisms with an antiseptic is recommended prior to surgery by several organizations, including the Centers for Disease Control and Prevention (CDC).[4,13-16] The purpose of the preoperative skin antisepsis is to reduce rapidly (within 10 minutes of application) the numbers of microorganisms within the surgical field prior to the wound incision and suppress regrowth for the duration of the surgical procedure and beyond.[17]

Two of the most commonly used active components in preoperative skin antisepsis are chlorhexidine gluconate and povidone iodine (PI). Another iodine-based skin disinfectant, iodine povacrylex in isopropyl alcohol, is commercially available.

It is generally recognized that chlorhexidine gluconate, although comparable with iodophors in terms of spectrum of antimicrobial activity, exhibits superiority in terms of a prolonged activity.[4,18] This confers an obvious advantage, especially for long-lasting surgical procedures.

In contrast with PI, the antimicrobial activity of chlorhexidine is not affected by the presence of body fluids.[19-21]

Rationale

The CDC recommends that 2% chlorhexidine-based preparations be used to cleanse the site of insertion of central venous and arterial catheters[22] but has not issued a recommendation as to which antiseptic should be used to prevent SSIs. On the contrary, chlorhexidine is recommended as skin antiseptic by Health Protection Scotland and the Canadian Patient Safety Institute.[14,15]

In 2010, a meta-analysis of 7 randomized controlled trials (RCTs) [23] (3,437 patients) was published, comparing chlorhexidine (0.5%-4%) with PI or other iodophors (0.7%-10%) for preoperative skin antisepsis. The use of chlorhexidine was associated with fewer SSIs (adjusted risk ratio, 0.64; 95% confidence interval [CI], 0.51-0.80) compared with iodine. In a cost-benefit model, sensitivity analysis documented that switching from iodine to chlorhexidine resulted in a net savings per surgical case of $16-$26.

Another meta-analysis of 6 RCTs comparing chlorhexidine (0.5%-4%) with PI for preoperative skin antisepsis yielded a pooled odds ratio of 0.68 (0.50-0.94, 95% CI; $P = .019$) for skin preparation with chlorhexidine versus PI.[24]

On the contrary, a review conducted in 2012 by Kamel et al[25] considering 3 skin antiseptics—iodophors, alcohol, or chlorhexidine gluconate, in any preparation—was unable to draw conclusions about which surgical site antiseptic is most effective for reducing SSIs.

Because new articles on the issue from 2012-2014 were published, we conducted an updated review.

Objectives

The aim of this review is to verify whether the most recent evidence supports the hypothesis that chlorhexidine used for perioperative antisepsis is more efficient than iodine compounds and other antiseptics in reducing the rate of SSIs. Furthermore, considering the relationship between cutaneous bacterial flora and SSI, we think it is necessary to evaluate the reduction of both. Therefore, we searched for studies, either RCTs or observational studies, in which the preoperative skin antisepsis with chlorhexidine was compared with antisepsis with other substances regarding the occurrence of SSI, the bacterial colonization, or both, in any kind of surgical procedure with cutaneous access and in any kind of patient.

We considered the primary end point of our review as the SSI incidence and the secondary end point as the skin bacterial colonization.

METHODS

Literature search strategy

The MEDLINE and Web of Science Core Collection databases were searched in July 2014 using the search terms *chlorhexidine AND (povidone iodine OR skin antisepsis OR surgical antisepsis OR preoperative antisepsis OR preoperative care OR preoperative preparation OR surgical infection OR wound infection OR healthcare acquired infection OR nosocomial infection OR hospital infection)*. The time span was from January 2000-July 2014 to reflect current clinical practice. All languages were searched.

Reference lists of retrieved reviews were browsed to identify additional relevant articles.

Selection criteria

Articles selected for inclusion in the review met the following criteria: (1) they were either RCTs or observational studies, both prospective or retrospective; (2) they compared preoperative chlorhexidine versus any other skin antiseptic; (3) they assessed for at least one of the outcomes of interest, SSI or skin bacterial colonization; (4) they assessed patients in whom the skin antisepsis was performed prior to surgery (ie, we retained studies in which skin bacterial colonization was the only outcome, but only if the study was performed in real practice, excluding studies performed on healthy volunteers); and (5) the surgical procedure, of every kind, was performed through cutaneous access. All types of patients were included. Studies evaluating chlorhexidine shower, bath, or foot bath prior to entry into the operating room were excluded for the purposes of this study. Noncomparative studies were excluded. So-called gray literature, such as conference abstracts, unpublished studies, or data obtained from personal communication, was not included.

Data analysis methods

Because of heterogeneity across the studies, results are partly described using a narrative approach; meta-analyses were conducted for comparable studies only, both for the outcome SSI incidence and for the outcome bacterial colonization rate. An appraisal of the quality of the evidence included in the meta-analysis, based on the GRADE (Grading of Recommendations Assessment, Development and Evaluation) criteria,[26] which includes, for each of the considered outcomes, quality of the study, inconsistency, indirectness, imprecision, and publication bias, was conducted.