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Review Article

Chlorhexidine-alcohol versus povidone-iodine for pre-operative skin preparation: A systematic review and meta-analysis

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ABSTRACT

Background: Surgical site infection (SSI) is a dreaded postoperative complication. Although preoperative skin cleansing in order to prevent surgical site infection (SSI) is standard surgical practice, there is clinical equipoise concerning whether povidone iodine (PI) or chlorhexidine alcohol (CHA) is the antiseptic agent of choice.
Objectives: To determine whether CHA or PI is the preferred preoperative skin preparation for reducing SSI in clean, clean-contaminated and contaminated surgery.
Search methods: PubMed, Embase, and gray literature sources were searched for randomized controlled trials (RCTs) comparing both CHA and PI between 1980 and 2014. Comparative RCTs of preoperative CHA versus PI studying SSI in clean, clean-contaminated and contaminated surgery were included. Risk of bias was assessed using Cochrane risk of bias.
Main result: We identified six eligible studies with an overall 2484 participants. The overall rate of SSI was 6.8% in the CHA group versus 11.0% in the PI group ($P < 0.0002$). CHA was superior to PI in the prevention of SSI with a pooled RR of 0.62 (95% CI, 0.48–0.81).
Conclusions: Preoperative surgical skin preparation with CHA is more effective than PI in preventing SSI across clean and clean-contaminated surgery. Further studies should evaluate the effectiveness of CHA versus PI in contaminated surgery.

1. Introduction

Surgical site infection (SSI) is a dreaded postoperative complication that affects approximately 5% of all patients undergoing surgery [1]. It is associated with prolonged length of hospital stay, prolonged postoperative recovery time, higher hospital readmission rates, and higher morbidity and mortality rates than patients without SSI [2]. The majority of SSIs are caused by contamination of a surgical incision with bacteria from the patient's own body [3].

There are several antiseptic skin cleansing agents available to the surgeon to use for patients undergoing clean, clean-contaminated, contaminated, and dirty surgery [3]. The traditional antiseptic cleansing agent of choice is povidone iodine (PI). It is cheap, effective, and the most commonly used agent of choice worldwide [4]. Chlorhexidine-alcohol (CHA) is a newer skin preparation agent, commonly composed of 2% chlorhexidine gluconate and 70% isopropyl alcohol [5]. Although more expensive than PI, it represents an alternative skin antiseptic agent, is reported to have a more rapid onset of action than PI and has persistent activity in the presence of body fluids [6]. In 2002, the CDC recommended the use of CHA prior to central venous and peripheral arterial catheterizations. CHA has recently been shown to be superior to PI in the prevention of SSI for clean surgery [7].

A recently performed Cochrane review did not reach a clear consensus on which antiseptic skin cleansing agent is associated with the lowest risk of SSI [8]. This study was performed in order to evaluate and synthesize existing evidence in the published literature concerning the role of PI and CHA in preventing SSIs in patients undergoing clean surgery.

2. Methods

A systematic review of randomized trials was undertaken according to PRISMA guidelines [9] to compare CHA versus PI in preventing SSI in patients undergoing clean, clean-contaminated, and contaminated surgery.

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Table 1
Characteristics of studies included in the meta-analysis of CHA versus PI in preventing SSI.

Reference	Year	Country	Sample size	Inclusion criteria	Exclusion criteria	Intervention	Control
Bibbo et al. [10]	2005	US	127	Clean surgery (elective foot and ankle surgery)	Open wounds, skin ulcers, active or chronic infection, antimicrobial therapy	4% Chlorhexidine in 70% isopropyl alcohol scrub for 7 minutes	7.5% Povidone iodine scrub for 7 minutes followed by 10% povidone-iodine paint
Paocharoen et al. [11]	2009	Thailand	500	Clean, clean-contaminated and contaminated wound	Dirty wound, uncontrolled diabetes, on immunosuppressive drugs, serum albumin less than 3.0 mg/dl	4% Chlorhexidine in 70% isopropyl alcohol followed by Hibitane scrub and paint	10% Povidone-iodine scrub followed by iodine solution
Saltzman et al. [12]	2009	US	100	Clean surgery (shoulder surgery)	Open wound, recurrent infection, or chronically immunosuppressed	2% Chlorhexidine in 70% isopropyl alcohol (ChloraPrep)	0.75% Povidone-iodine scrub followed by 1.0% iodine paint
Sistla et al. [13]	2010	India	400	Clean surgery (inguinal hernia repair)	Recurrent or complicated inguinal hernia	2.5% Chlorhexidine in 70% ethanol	10% Povidone-iodine
Darouiche et al. [7]	2010	US	849	Clean-contaminated surgery	Evidence of infection or adjacent to the operation site	2% Chlorhexidine gluconate in 70% isopropyl alcohol	10% Povidone iodine
Patil et al. [14]	2013	India	508	Clean and clean-contaminated surgery	Contaminated and dirty wounds, evidence of infection adjacent to operative site	2.5% Chlorhexidine gluconate in 63% isopropyl alcohol	5% Povidone-iodine

2.1. Literature search

An electronic literature search was conducted in July 2014 using the following three databases of scientific literature: EMBASE, PubMed and the Cochrane. The search strategy was developed by an experienced librarian in conjunction with a clinical researcher. The search strategy used the following medical subject heading (MeSH) terms: chlorhexidine-alcohol OR chlorhexidine-isopropyl OR chloraprep OR iodine OR povidone-iodine OR betadine OR iodophor AND surgical site infection OR SSI OR wound infection.

No restrictions were applied on language, the type of risk factor, age, or gender of the subject. All abstracts that met our search strategy were examined. To limit publication bias, the references of all primary studies were also hand searched for studies potentially missed in the electronic search. In addition we searched gray literature sources, including OpenGray and the NLM gateway. We personally communicated with authors where necessary. For studies not published in English we used Google Translate to translate relevant journals to English. All shortlisted titles and abstracts were downloaded to a reference manager (EndNote) for detection of duplicates. In addition, a researcher manually checked this list for duplicates.

2.2. Study selection

This review was planned, conducted and reported in adherence to the PRISMA guidelines. Our inclusion criteria included all RCTs that reported the rate of postoperative SSI in patients who have undergone clean, clean contaminated, and contaminated surgery to any part of the body. We excluded non-randomized trials, studies with incomplete method selection, studies that did not compare CHA with PI, studies that did not measure SSI, duplicate publications and narrative reviews. Two reviewers performed eligibility assessment independently by assessing titles and abstracts of citations identified by the search databases results. Any differences between the reviewers were resolved by discussion and mutual agreement.

2.3. Data extraction

Information of the included studies was extracted for analysis using piloted data forms. The extracted information includes study ID, year, country, design, number of participants, intervention, comparison, and primary and secondary outcomes. The primary outcome was postoperative SSI. The secondary outcome was bacterial decolonization.

See Table 1 for characteristics of studies included in the meta-analysis of CHA versus PI in preventing SSI, and Table 2 for primary and secondary outcomes.

2.4. Quality assessment

Risk of bias was assessed by considering randomization procedure, allocation concealment, blinding, and data completion using the Cochrane Collaboration's tool for assessing risk of bias [15]. These items were classified as low, unclear, or high according to risk (see Table 3 for risk of bias).

2.5. Data analysis

Data were entered into Microsoft Office Excel sheets for analysis. Statistical analysis was performed using Stata Version 13.1. Relative risk was calculated (95% CI) for primary outcomes using a random effect model. Standard Chi-square and I^2 test were used to assess for heterogeneity.

3. Results

3.1. Literature search

The search identified fifty-three relevant studies. After applying exclusion criteria, six studies were eligible for meta-analysis (Fig. 1). Details of the included trials are summarized in Table 1.

3.2. Characteristics of studies included in the final analysis

All six studies compared CHA versus PI in preventing SSI. CHA concentration was similar across all studies and ranged from 2% to 4% of chlorhexidine, and 63% to 70% of alcohol. PI concentration ranged from 5% to 10%. The method in which these skin preparing agents were applied on the skin was different; three studies by Bibbo et al. [10], Saltzman et al. [12] and Sistla et al. [13] used simple painting, two studies by Paocharoen et al. [11] and Darouiche et al. [7] used scrubbing and painting, and one study by Patil et al. [14] did not mention an application method. All studies reported that preoperative skin preparation with CHA is more efficient than PI in preventing SSI (Table 2: primary and secondary outcomes).