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Abstract

Background:

A patient's skin is the major source of pathogens that can cause post-operative complications such as surgical site infections (SSIs). Optimization of pre-operative skin antisepsis is obtained with chlorhexidine gluconate (CG) and povidone-iodine (PI). These two solutions are the most widely used antiseptics for pre-operative purposes.

Objective:

Among surgical patients greater than 18 years of age undergoing clean-contaminated surgery, which antiseptic, iodophors or chlorhexidine gluconate, is more effective at reducing postoperative surgical site infections?

Methods:

A search was done in PubMed utilizing the terms chlorhexidine, infection control, iodophors, and surgical site infection. The limits applied included randomized controlled trial, published within 10 years, and humans.

Results:

Darouiche et al found that the application of 2% CG reduced the incidence of SSIs by 41% compared to 10% PI. This study demonstrated statistical significance ($p = 0.0049$). Bibi et al

found a 45.4% reduction in SSI rates with the use of 2% CG compared to 10% PI but was not statistically significant (p =0.3961). Park et al found no difference between 2% CG and 10% PI regarding the reduction of SSIs (p= 0.8532).

Conclusion:

There is not a significant difference between the rates of SSIs when using CG compared to PI in the setting of clean-contaminated surgeries. Future research should be conducted to determine if a significant difference is present, and if there is a difference in efficacy of antiseptics in the settings of clean and contaminated wounds. CG and PI may be used interchangeably depending on presence of allergy, cost, and convenience.

Introduction

A surgical patient's skin is the major source of pathogens that contribute to surgical site infections (SSIs). Most SSIs are caused by endogenous pathogens which are the patient's native bacteria inhabiting the skin and body. Exogenous pathogens are those that come from an outside source such as unsterile surgical equipment or contaminants found in the air. SSIs are categorized as superficial incisional, deep incisional, or organ/space. [1] Incisional infections often manifest as cellulitis while deeper infections develop into abscesses. The degree of risk for infection post-operatively depends on the type of surgical wound involved. Clean-contaminated wounds have no evidence of infection at the time of surgery but involve operating on an internal organ. Other factors that increase risk for SSIs are diabetes, obesity, old age, weakened immune system, and cancer. [1]

Antimicrobial skin preparations are used before surgery as a means to reduce SSIs by reducing the endogenous pathogens on a patient's skin. SSIs effect 300,000 to 500,000 surgical patients in

the United States each year and account for 29% of nosocomial infections.[2] These infections necessitate the use of costly hospital resources, extend inpatient stays, and carry an increased potential for morbidity and mortality.[2] Antimicrobials may be bactericidal or bacteriostatic. Bactericidals work by killing the microorganisms that they come into contact with while bacteriostatics inhibit the growth of microorganisms.

Two standard antimicrobial compounds used for pre-surgical skin preparation are chlorhexidine gluconate (CG) and povidone-iodine (PI). These compounds are bactericidal, therefore, they rapidly reduce the number of transient and resident microorganisms in the surgical field as well as suppress rebound growth for several hours after application.[3] The solutions applied to the skin prior to surgical incision, CG and PI, are used about equally across the United States and may be in an aqueous or alcoholic solution with varying concentrations. Our study aims to compare the efficacy of 2% chlorhexidine gluconate solutions to 10% povidone–iodine solutions regarding the prevention of post-operative SSIs in adult patients within 30 days of undergoing a clean-contaminated surgery.

Methods

PubMed was the only database used to find the articles for this study. The search was performed using the terms chlorhexidine, infection control, iodophors, and surgical site infection. The limits used for the search included “randomized controlled trial, published within 10 years, and humans”. This search resulted in 66 results of which 10 were chosen to investigate further. Of the 10, three were determined to have met the inclusion and exclusion criteria seen in Table 1. Each study was reviewed to identify the presence of relative risk statistics or data needed to calculate relative risks.

Table 1. Inclusion and Exclusion Criteria of Studies Accepted For Systemic Review	
Inclusion Criteria	Exclusion Criteria
-18+ Years Old -Concentration of 2% Chlorhexidine Gluconate Solution -Concentration of 7.5% or 10% Povidone – Iodine Solution -Clean-Contaminated Surgery -30 Day Observation Period Post-Surgery	- <18 Years Old -Less than 30 days of follow-up -Non-comparable concentrations of antiseptics -Clean, Contaminated, or Dirty Surgery

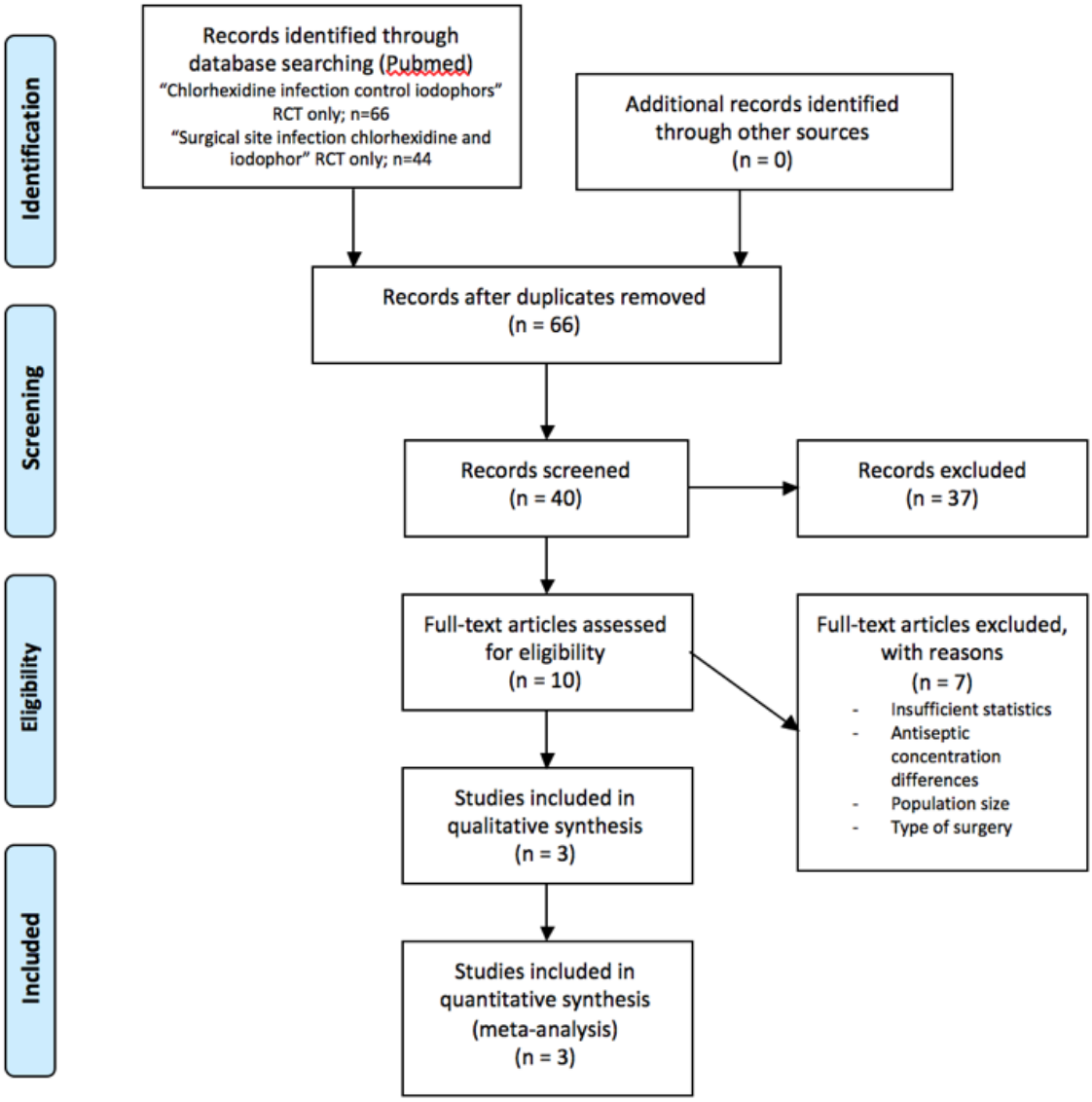

Figure 1. Prisma Flow Chart

Results

Study 1

Chlorhexidine–Alcohol versus Povidone–Iodine for Surgical-Site Antisepsis.[2]

Objective:

"To compare the efficacy of chlorhexidine–alcohol with that of povidone–iodine for preventing surgical-site infections".[2]

Study Design:

This randomized control trial was conducted at six university affiliated hospitals in the United States.

Table 2. Inclusion and Exclusion Criteria of Study 1	
Inclusion Criteria	Exclusion criteria
-Patients 18 years of age -Undergoing clean-contaminated surgery	-History of allergy to chlorhexidine, alcohol, iodophors. -Evidence of infection at or adjacent to the operative site. -The perceived inability to follow the patient's course for 30 days after surgery

Patients were randomly assigned in a 1:1 ratio to have the skin at the surgical site prepped with a 2% chlorhexidine gluconate solution or a 10% povidone-iodine solution. Randomization was achieved with the use of computer-generated sorting with no blocking. This system helped to address potential interhospital differences with the two groups. The operating surgeon only became aware of the intervention when the patient entered the operating room.

The first group was preoperatively scrubbed with ChloraPrep (2% chlorhexidine gluconate and 70% isopropyl alcohol). If the area exceeded 33cm x 33cm, more than one applicator was used.

The second group was preoperatively scrubbed and then painted with a Scrub Care Skin Prep Tray (aqueous solution of 10% povidone–iodine).

The outcome of the study was measured by the presence of surgical site infections within 30 days after surgery. Secondary outcomes included the specific type of surgical site infection present differentiated into "superficial incisional infection (which involved only skin and subcutaneous tissue and excluded stitch-related abscesses), deep incisional infection (which involved fascia and muscle), or organ-space infection (which involved any organ or space other than the incised layer of body wall that was opened or manipulated during the operation)" [2]

Study results:

A total of 849 qualified participants were included in the study; 409 used the chlorhexidine-alcohol solution, and 440 used povidone-iodine solution. Of the total 897 participants, 36 were excluded from the per-protocol analysis: "25 underwent clean rather than clean-contaminated surgery, 4 dropped out of the study 1 or 2 days after surgery, and 7 died before completion of the 30-day follow-up (4 in the chlorhexidine–alcohol group and 3 in the povidone–iodine group)".

Each patient was given systemic prophylactic antibiotics one hour before the first incision. "For the patients in the intention-to-treat population, the overall rate of surgical-site infection was significantly lower in the chlorhexidine–alcohol group (9.5%) than in the povidone–iodine group (16.1%, P=0.004)".

Additionally, chlorhexidine-alcohol was associated with fewer secondary superficial incisional infections (relative risk, 0.48; 95% CI, 0.28 to 0.84) and deep incisional infections (relative risk, 0.33; 95% CI, 0.11 to 1.01). There was no difference between organ-space infection and sepsis from SSI. [2]

Study Critique:

A large number of participants and high rate of compliance were major strengths of this study. The study also accounted for variability in many aspects such as systemic prophylactic antibiotics in which there was no significant difference in type or number of antibiotics used; assessing the effects between group and surgery type, which was found to be not significant; and a Breslow-Day test indicated no significant difference between the incidence of either any type of surgical-site infection (P=0.35) or individual types of infection (P≥0.19). [2]

Study 2

Is chlorhexidine-gluconate superior than Povidone-Iodine in preventing surgical site infections? A multicenter study. [4]

Objective:

"To compare the efficacy of povidone-iodine and chlorhexidine gluconate scrubs in preventing surgical site infections".[4]

Study Design:

A randomized control trial was conducted in two major public sector hospitals in Karachi and Islamabad, Pakistan. [4]

Table 3. Inclusion and Exclusion Criteria of Study 2	
Inclusion Criteria	Exclusion Criteria
-Patients 18-60 years old -Undergoing clean or contaminated surgery	-Diabetes -Infection adjacent to surgical site -Undergoing emergency surgery and unwilling to participate

A total of 400 participants were included in this study: 200 from a general surgery unit at Jinnah Postgraduate Medical Centre and 200 from a surgical unit at Pakistan institute of Medical Sciences. A predesigned proforma was used to record the patient's surgical procedure, prophylactic antibiotics, and pre-surgical antiseptic agent. A day before surgery patients were randomly assigned to one of the treatment groups. Randomization was done by lottery ticket method where the investigator picked slips for each patient. Group I was comprised of patients scrubbed with 10% povidone- iodine, and group II was scrubbed with 2% chlorhexidine-gluconate in 70% isopropyl alcohol. The operating surgeon and staff knew which surgical preparation was being used.

All patients were monitored daily for any sign of surgical site infection post-surgery. They used the Center of Disease Control's definition which states, "Infection would be regarded as surgical site infection if it occurs within 30 days of procedure and has at least one of the following symptoms; purulent drainage from the wound, pain or tenderness, localized swelling, redness, malodor, or fever". Patients visited the outpatient department weekly after discharge to assess for SSIs. [4]

Study Results:

Of the 400 participants, 352 completed the study. Group I had 207 participants, and group II had 151 participants. "Overall, 22 (10%) patients developed SSI in group I, while 12 (7.1%) patients from group II developed SSI during follow-up. Although infection rates were lower in group II compared to group I, intention-to-treat analysis showed that this difference was not statistically significant (p=0.324)".[1] Additionally, the use of prophylactic antibiotics in both groups showed no statistically significant difference. [4]

Study Critique:

There was a large discrepancy in the size of each study group. To make up for this, additional analysis was completed (p-values, chi-squared test). A strength of this study was the exclusion criteria which controlled confounding variables such as high-risk groups and prophylactic antibiotics.

Study 3

Randomized clinical trial of preoperative skin antisepsis with chlorhexidine gluconate or povidone–iodine.[3]

Objective:

Compare the efficacy of chlorhexidine gluconate and povidone-iodine on surgical site infections in clean-contaminated abdominal surgery. [3]

Study design:

This randomized study took place in Korea, but the specific region or facility is not noted.

Table 4. Inclusion and Exclusion Criteria of Study 3	
Inclusion Criteria	Exclusion Criteria
-Undergoing hepatobiliary–pancreatic (HBP) surgery	-Allergy to chlorhexidine or povidone -Taking an immunosuppressant -Uncontrolled diabetes mellitus -BMI > 30kg/m^2

Patients undergoing clean-contaminated upper gastrointestinal or hepatobiliary–pancreatic open surgery between 2011 and 2014 were assigned to be preoperatively scrubbed with chlorhexidine gluconate or povidone–iodine. Before surgery, patients in the CG group were soaped with 4% CG and then painted with 2% solution of CG. Patients in the PI group were soaped with 7.5% PI and then painted with a 10% aqueous solution. After three minutes of drying, the surgical nurse dried the skin with a sterile fabric towel.

All patients were given preoperative antibiotics within one hour of skin incision. Monitoring for SSIs began 48 hours post-operatively. "The primary endpoint was the occurrence of SSI within 30 days of surgery. Secondary endpoints included causative organisms and risk factors for SSI." This study defined SSI as, "infection arising from a surgical procedure and occurring within 30 days of surgery" [3]

Study Results:

Of the 597 participants, 534 were included in the study, and the study groups were equal in size. The overall SSI rate was 5.8%; superficial SSI developed in 9 patients, deep SSI in 12 patients, and organ-space SSI in ten patients. There was no different in overall rate of SSIs between the CG group and PI group. Of the CG group, 15 of 267 (5.6%) experienced SSI and of the PI group, 16 of 267 (6.0%; P =0.853) experienced SSI. [3]

Study critique:

The aqueous solution was patted dry which may have decreased the sustained bactericidal effect. This study had a limited scope of surgeries as the SSI rate was only evaluated for upper gastrointestinal or hepatobiliary operations.

Discussion

Darouiche et al found that the application of 2% CG reduced the incidence of SSIs by 41% compared to 10% PI. This study demonstrated statistical significance as seen in table 5. ($p = 0.0049$). The superior clinical efficacy is likely due to its more rapid onset of action, persistent activity, and residual effect. Bibi et al found a 45.4% reduction in SSI rates with the use of 2% CG compared to 10% PI but was not statistically significant (table 5). Park et al found no difference between 2% CG and 10% PI on reduction of SSIs. This could be due to the rate of SSIs in this study being low overall. Additionally, the 2% CG was patted dry to shorten the dry time but may have decreased the sustained bactericidal effect.

Some limitations were noted between the three studies chosen. The first included differences in application of 2% CG and 10% PI. A step-by-step approach was not provided to ensure all application processes were identical which could have resulted in confounding variables. Some patients were “scrubbed” and others “painted” or “soaped” with the exact mechanism undisclosed. Additionally, Darouiche et al and Bibi et al used 10% PI solutions whereas Park et al used an aqueous 10% PI solution. Effectiveness against SSIs regarding different types of solutions is unknown. Each study was completed in a different country (Pakistan, United States, and Korea). The protocols and standards upheld at each institution are not known. Park et al did not disclose information of the facility where surgery took place or where patients were treated

and monitored post-operatively. Dariouche et al allowed hospitals to continue their pre-existing practices such as pre-operative showering which could alter the efficacy of 2% CG and 10% PI. Finally, the prevalence of the most common SSI microbiological flora may differ from each facility/country where each study was conducted.

Limited biases were found due to adequate blinding. One potential source of bias was included in Park et al where the surgeon was made aware of the pre-operative intervention applied. All other surgeons were blinded until the patient entered the operating room.

Strengths of the studies included large sample sizes (849, 352, 534) with near equivalent study participants in each CG and PI group. Each study applied respectable exclusion criteria to rule out comorbidities that could have significant effects on the results. Each study used the same concentration of 2% CG and 10% PI and only included clean-contaminated surgeries.

Table 5. Comparison of Statistical Analysis of Studies.

	Antiseptic Solution	**Relative Risk**	**95% Confidence Interval**	**P-Value**
Study 1	Chlorhexidine-Gluconate	0.59	0.41-0.85	0.0049
	Povidone-Iodine	1.7	1.17-2.44	0.0049
Study 2	Chlorhexidine-Gluconate	0.75	0.38-1.5	0.3961
	Povidone-Iodine	1.3	0.68-2.6	0.3961
Study 3	Chlorhexidine-Gluconate	0.93	0.47-1.9	0.8532
	Povidone-Iodine	1.1	0.54-2.1	0.8532

Conclusion

Given the limited research currently available, there is not a significant difference between the rate of SSIs when using CG or PI in the setting of clean-contaminated surgeries. More research needs to be conducted to further evaluate if one of these skin antiseptics is significantly more efficacious than the other. Future studies should be done on these antiseptics in the settings of clean and contaminated wounds in addition to the previously studied clean-contaminated for a broader scope of research.

Because no significant difference between the SSI rate and CG or PI has been identified at this time, the antiseptics may be used interchangeably depending on allergy, cost, and convenience. Allergies to PI and CG have both been identified in patients. However, there is no cross-reactivity between these two antiseptics so a patient with an allergy to one may readily try the other. [5]

Regarding cost, the antiseptic with a better value per volume should be chosen. This will allow for a competitive market leading to control over antiseptic costs and will allow hospitals to keep costs down. The convenience of available antiseptics should also be taken into account when selecting an agent for skin antisepsis. This is especially important in the setting of non-elective surgeries when time cannot be wasted.

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