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Impact of choice of skin preparation solution in cardiac surgery on rate of surgical site infection: a propensity score matched analysis

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Abstract

Background: Antiseptic skin preparations containing chlorhexidine gluconate and povidone iodine are routinely used to reduce the risk of surgical site infection (SSI). This study assesses the efficacy of two alcohol-based solutions, 2% chlorhexidine-alcohol and 10% povidone iodine-alcohol, on the incidence of cardiac SSI.

Methods: A total of 738 consecutive patients undergoing cardiac surgery had skin preparation with 2% chlorhexidine gluconate in 70% isopropanol (ChloraPrep, BD Ltd, UK) were propensity matched to 738 patients with skin prepared with 10% povidone–iodine in 30% industrial methylated spirit (Videne Alcoholic Tincture, Ecolab Ltd, UK). Continuous, prospective SSI surveillance data were collected for all these patients. A retrospective analysis of prospectively collected perioperative data was performed.

Results: The overall rate of SSI was similar in the chlorhexidine–alcohol and povidone–iodine–alcohol groups (3.3% versus 3.8%; *P* = 0.14; relative risk [RR] = 0.98; 95% confidence interval [CI] = 0.52–1.78). Superficial (1.2% versus 1.8%; *P* = 0.18; RR = 0.97; 95% CI = 0.48–1.80) and deep incisional (1.2% versus 1.6%; *P* = 0.24) SSI rates were also similar with 10% povidone–iodine–alcohol being marginally more effective against organ-space infections (0.8% versus 0.4%; *P* = 0.05; RR = 0.38; 95% CI = 0.20–1.01).

Conclusion: Our analysis confirms that alcohol-based skin preparation in cardiac surgery with povidone–iodine reduces the incidence of organ-space infections with no significant superiority in preventing incisional SSI compared with chlorhexidine-alcohol.

Keywords

Audit, surgical site infection, surveillance

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Introduction

Despite recent advances in prevention and perioperative care, surgical site infection (SSI) remains a pressing concern in cardiac surgery due to its considerable impact on in-hospital mortality, morbidity and utilisation of resources. Skin antisepsis has been a well-recognised strategy to reduce SSI. Antiseptic skin preparations containing chlorhexidine and povidone iodine are routinely used. In recent years, 2% chlorhexidine in 70% isopropanol has attracted considerable attention through several prominent clinical studies suggesting its protective effect against both catheter-related bloodstream infections (CR-BSIs) during insertion

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of vascular catheters and SSIs during clean-contaminated surgery (i.e. colorectal, small intestinal, gastroesophageal, biliary, thoracic, gynaecologic or urologic operations performed under controlled conditions without substantial spillage or unusual contamination) (Darouiche et al., 2010; Lee et al., 2010; Noorani et al., 2010; Pronovost et al., 2006; Ruschulte et al., 2009). Preference for chlorhexidine gluconate, in particular over its main competitor, povidone–iodine, has been expressed in several practice recommendations and evidence-based guidelines for skin antisepsis, though the role of alcohol in formulations is often forgotten (Maiwald and Chan, 2010). Most studies which support practice guidance have looked at the use of chlorhexidine for skin antisepsis to prevent CR-BSIs, where comparisons of chlorhexidine-alcohol formulations with aqueous-based solutions or solutions with alcohol alone have demonstrated differences in infection rates. Studies looking at the impact of chlorhexidine-alcohol for the prevention of SSIs in surgical settings are limited, and those that exist often neglect to address the role of alcohol (Darouiche et al., 2010). Currently, there are no studies comparing 2% chlorhexidine-alcohol with 10% povidone–iodine–alcohol for skin antisepsis in cardiac surgery. The aim of this study is to assess the efficacy of these two skin preparation solutions on incidence of SSI after cardiac surgery in a recent cohort of patients.

Materials and methods

Study sample

This study comprised a retrospective analysis of a prospectively collected cardiac surgery database (PATS; Dendrite Clinical Systems, Ltd, Oxford, UK) as well as continuous, prospective infection surveillance data of patients that underwent cardiac surgery at two institutions from January 2013 to October 2015. The study was approved by the institutional ethics committee and informed consent was waived for this study due to its retrospective nature. The PATS database captures detailed information on a wide range of preoperative, intraoperative and hospital postoperative variables (including complications and mortality) for all patients undergoing cardiac surgery in our institution. The database was collected and reported in accordance with the Society for Cardiothoracic Surgery in Great Britain & Ireland database criteria. Data on SSI were collected via prospective, continuous surveillance by trained surveillance nurses using Public Health England (PHE) 2013 protocol for surgical site infection surveillance. All classifications of SSI (sternal and donor) detected on primary admission or readmission were included. Superficial incisional SSI were recorded up to 30 days following surgery. Deep incisional and organ-space SSI were included up to one year following surgery, in line with PHE protocol for the presence of implant as stainless-steel sternal wires are used in median sternotomy cases. From January 2013 to October 2015, 738 patients underwent cardiac surgery with skin preparation using 2% chlorhexidine gluconate in 70% isopropanol (ChloraPrep, BD Ltd, UK). During the same period, 1486 patients underwent cardiac surgery with skin preparation using 10% povidone–iodine in 30% industrial methylated spirit (Videne Alcoholic Tinture, Ecolab Ltd, UK).

Intervention

The skin preparation solution with alcohol was selected based on hospital site, operator preference and patient allergies. The skin at the surgical site was either preoperatively scrubbed with an applicator that contained 2% chlorhexidine gluconate in 70% isopropyl alcohol or preoperatively painted with 10% povidone–iodine in 30% industrial methylated spirit, applied with a sterile swab in a sterile Rampley's Sponge Holder using a sterile gallie pot. This was performed in conjunction with a sterile swab pre-prep involving multiple swabs being separately dedicated to the chest and lower extremities. Both techniques started from the incision site moving towards the periphery. More than one 2% chlorhexidine gluconate in 70% isopropanol 26 mL applicator was used if the coverage area exceeded 33 × 33 cm.

Variables and data collection

Preoperative variables of interest included age, gender, smoking history, chronic obstructive pulmonary disease, diabetes, hypercholesterolemia, renal insufficiency (preoperative serum creatinine $\geq 200\ \mu mol \cdot L^{-1}$), body mass index, hypertension, peripheral vascular disease, cerebrovascular disease, left ventricular ejection fraction and urgency (operation performed < 24 h versus > 24 h from time of referral). Intraoperative variable of interest included use of bilateral internal mammary arteries (IMAs). Postoperative variables of interest included any SSI: superficial incisional infection; deep incisional infection; and organ-space infection.

Statistical analysis

Patients who underwent cardiac surgery with skin preparation using chlorhexidine–alcohol were compared with those who had skin preparation using povidone–iodine–alcohol using *t*-tests and Kruskal–Wallis tests for continuous variables and Chi-squared tests for categorical variables. A propensity analysis was performed modelling the probability of receiving chlorhexidine–alcohol. Briefly, a non-parsimonious multivariate logistic regression model using clinically relevant variables was generated to compute a propensity score for each patient (Table 1). All clinically relevant variables were included in the model. The propensity score (or probability of receiving

Table 1. Logistic regression model to generate propensity scores for chlorhexidine group (n = 738) versus povidone–iodine group (n = 1486).

		95% Wald confidence limits		
Effect	Point estimate	Lower	Upper	*P* value
< 60 years	0.79	0.69	1.12	0.23
60–74 years	0.77	0.68	1.04	0.19
> 75 years	0.79	0.60	1.12	0.21
Gender	0.75	0.60	1.05	0.20
Diabetes	0.79	0.61	1.09	0.17
Hypertension	1.11	0.98	1.66	0.49
Hypercholesterolemia	1.55	1.23	2.11	0.56
PVD	0.80	0.66	1.11	0.23
BMI < 30	0.84	0.68	1.25	0.36
BMI ≥ 30	0.73	0.58	1.03	0.43
Previous stroke/TIA	1.11	0.83	1.99	0.64
COPD	0.99	0.73	1.35	0.41
Creatinine ≥ 200 μmol·L^{-1}	0.94	0.76	1.12	0.24
LVEF > 49%	1.75	1.43	2.32	0.59
LVEF 30–49%	0.88	0.60	1.29	0.22
LVEF < 30%	1.45	1.33	1.92	0.43
Elective	0.72	0.67	1.03	0.21
Urgent	0.67	0.48	1.01	0.22
Emergency	1.61	1.90	2.16	0.47
BIMA	1.11	0.95	1.55	0.48

BIMA, bilateral internal mammary arteries; BMI, body mass index; COPD, chronic obstructive pulmonary disease; LVEF, left ventricle ejection fraction; PVD, peripheral vascular disease; TIA, transient ischemic attack.

chlorhexidine–alcohol) was then used to obtain a one-to-one match of all chlorhexidine–alcohol cases with povidone–iodine–alcohol by a 'greedy matching' technique (Parsons, 2001). The outcomes of interest were compared between these matched groups.

Logistic regression was used to examine the association of chlorhexidine–alcohol usage with SSI after adjusting for differences between patients on the basis of each of the abovementioned preoperative variables. Statistical significance was indicated by a two-tailed P value < 0.05. All analyses were performed with the Statistical Analysis Systems software package (Release 9.4; SAS Institute, Cary, NC, USA). The authors had full access to the data and take responsibility for its integrity. All authors have read and agree to the manuscript as written.

Results

A total of 2224 patients formed the initial study population. Compared to patients who had skin preparation with chlorhexidine–alcohol, those with skin preparation with povidone–iodine–alcohol were more likely to be female, and more likely to have diabetes, hypercholesterolemia, renal insufficiency, hypertension and peripheral vascular disease (Table 2). Patients who had skin antisepsis with skin preparation with povidone–iodine–alcohol also received more bilateral IMAs than the chlorhexidine–alcohol group (14.1% versus 9.3%; $P = 0.001$). The overall SSI rate for the entire cohort was 3.2%.

The propensity score model included 20 patient variables that are listed along with their confidence intervals in Table 1. The *c* statistic for this model was 0.81 (Hosmer-Lemeshow

Table 2. A total of 2224 unmatched cases: patient characteristics of chlorhexidine group vs. povidone–iodine group.

Demographics	Chlorhexidine group (n = 738 (%))	Povidone group (n = 1486 (%))	*P* value
< 60 years	156 (21.2)	278 (18.7)	0.08
60–74 years	289 (39.1)	645 (43.4)	0.78
> 75 years	293 (39.7)	563 (37.9)	0.90
Gender	168 (22.8)	586 (39.4)	0.0001
Diabetes	256 (34.7)	632 (42.5)	0.001
Hypertension	254 (34.4)	618 (41.6)	0.003
Hypercholesterolemia	242 (32.8)	598 (40.2)	0.002
PVD	76 (10.3)	186 (12.5)	0.01
BMI < 30	589 (79.8)	1147 (77.2)	0.89
BMI ≥ 30	149 (20.2)	339 (22.8)	0.76
Previous stroke/TIA	43 (5.8)	92 (6.2)	0.92
COPD	78 (10.6)	160 (10.9)	0.96
Creatinine ≥ 200 μmol·L^{-1}	47 (6.4)	138 (9.3)	0.04
LVEF > 49%	432 (58.5)	898 (60.4)	0.90
LVEF 30–49%	182 (24.7)	312 (21.0)	0.88
LVEF < 30%	124 (16.8)	276 (18.6)	0.84
Elective	449 (67.6)	998 (67.2)	0.96
Urgent	201 (27.2)	387 (26.0)	0.78
Emergency	38 (5.2)	101 (6.8)	0.69
BIMA	69 (9.3)	209 (14.1)	0.001

BIMA, bilateral internal mammary arteries; BMI, body mass index; COPD, chronic obstructive pulmonary disease; LVEF, left ventricle ejection fraction; PVD, peripheral vascular disease; TIA, transient ischemic attack.

goodness-of-fit $P = 0.3057$). All 738 chlorhexidine–alcohol cases could be matched to 738 povidone–iodine–alcohol patients. The two groups were well matched for all the patient variables (Table 3).

After adjusting for clinical covariates, the overall rate of SSI was similar in the chlorhexidine–alcohol group and povidone–iodine–alcohol group (3.3% versus 3.8%; $P = 0.14$; relative risk [RR] = 0.98; 95% confidence interval [CI] = 0.52–1.78). The rates of superficial incisional infections (1.2% versus 1.8%; $P = 0.18$; RR = 0.97; 95% CI = 0.48–1.80) and deep incisional infections (1.2% versus 1.6%; $P = 0.24$) were also similar with povidone–iodine–alcohol being marginally more protective against organ-space infections (0.8% versus 0.4%; $P = 0.05$; RR = 0.38; 95% CI = 0.20–1.01).

Discussion

The results of our study demonstrate that use of chlorhexidine–alcohol and povidone–iodine–alcohol as skin preparation solution in cardiac surgery is associated with similar SSI rate with marginally reduced organ-space infection rate in povidone–iodine–alcohol patients. A large volume of data reporting the superiority of 2% chlorhexidine gluconate in 70% isopropyl alcohol as a skin preparation solution has emerged recently, particularly for skin antisepsis prior to vascular catheter insertion (Darouiche et al., 2010; Lee et al., 2010; Noorani et al., 2010; Pronovost et al., 2006; Ruschulte et al., 2010). Studies supporting the use of 2% chlorhexidine gluconate in 70% isopropanol in surgical settings are limited and the role of alcohol in antiseptic formulations is missed, as no distinction is made between solutions containing isopropanol and those that do not and the effect on SSIs being solely attributed to chlorhexidine, thus making these comparisons not valid (Maiwald and Chan, 2012). The superiority of chlorhexidine–alcohol is related to rapid action of the isopropanol, persistent activity despite exposure to bodily fluids and residual effect (Darouiche et al., 2010). Similarly, there is

Table 3. A total of 1476 matched cases: patient characteristics of chlorhexidine group vs. povidone–iodine group.

Demographics	Chlorhexidine group (n = 738 (%))	Povidone group (n = 738 (%))	*P* value
< 60 years	156 (21.2)	169 (22.9)	0.84
60–74 years	289 (39.1)	301 (40.8)	0.78
> 75 years	293 (39.7)	268 (36.3)	0.64
Gender	168 (22.8)	187 (25.3)	0.48
Diabetes	256 (34.7)	268 (36.3)	0.67
Hypertension	254 (34.4)	271 (36.7)	0.73
Hypercholesterolemia	242 (32.8)	245 (33.2)	0.79
PVD	76 (10.3)	71 (9.6)	0.83
BMI < 30	589 (79.8)	593 (80.4)	0.86
BMI ≥ 30	149 (20.2)	145 (19.6)	0.92
Previous stroke/TIA	43 (5.8)	46 (6.2)	0.88
COPD	78 (10.6)	81 (10.9)	0.96
Creatinine ≥ 200 μmol·L^{-1}	47 (6.4)	51 (6.9)	0.89
LVEF > 49%	432 (58.5)	448 (60.7)	0.74
LVEF 30–49%	182 (24.7)	181 (24.5)	0.94
LVEF < 30%	124 (16.8)	109 (14.8)	0.64
Elective	499 (67.6)	488 (66.1)	0.88
Urgent	201 (27.2)	207 (28.0)	0.76
Emergency	38 (5.2)	43 (5.8)	0.88
BIMA	69 (9.3)	74 (10.0)	0.72

BIMA, bilateral internal mammary arteries; BMI, body mass index; COPD, chronic obstructive pulmonary disease; LVEF, left ventricle ejection fraction; PVD, peripheral vascular disease; TIA, transient ischemic attack.

abundant evidence to validate the safety and efficacy of alcohol-based povidone–iodine (Dumville et al., 2015; Swenson et al., 2009). However, to date a comparative study reporting rates of SSI in cardiac surgery using these two aforementioned antiseptic solutions has not been carried out and therefore the cardiac experience is not reflected in recent global guidance (World Health Organization, 2016). This study is unique as it the largest reported clinical experience to date of skin preparation in cardiac surgery comparing alcohol-based solutions (chlorhexidine–alcohol and povidone–iodine–alcohol) and confirms that contrary to published experience reporting superiority of 2% chlorhexidine gluconate in 70% isopropanol, there is no significant protective effect of this antiseptic solution in reducing SSI rates after cardiac surgery compared with 10% povidone–iodine in 30% industrial methylated spirit. This finding reinforces our previous work using multiple logistic regression to investigate risk factors in CABG SSI, which showed no significant difference between these skin preparation solutions ($P = 0.403$) (Rochon and Jarman, 2013).

We have attempted to make meaningful comparisons between the chlorhexidine–alcohol group and a contemporaneous group of povidone–iodine–alcohol prepped patients. To do this, we have used two statistical approaches based on propensity modelling, a technique that has been strongly advocated in several recent publications (Austin, 2010) in an effort to better evaluate treatment comparisons from nonrandomized clinical experiences. The propensity score is the probability of a patient receiving a given intervention (in this case 2% chlorhexidine gluconate) based on a non-parsimonious model derived from preoperative patient variables. The propensity model thus reduces many variables to a single balancing score, facilitating meaningful intergroup comparisons. We used two approaches, namely the creation of matched pairs based on propensity

score and logistic regression analysis of outcomes in which propensity score participated as a variable.

Using the propensity-matching technique, the 2% chlorhexidine–alcohol and 10% povidone–iodine–alcohol groups were remarkably well-matched in terms of known risk predictors of outcomes after cardiac surgery. The overall SSI rates between groups were not statistically different. However, there was a marginally reduced rate of organ-space infection in the povidone–iodine–alcohol group. The most plausible explanation for this is that whereas there is good evidence favouring chlorhexidine gluconate-alcohol combinations over aqueous povidone–iodine, the most commonly tested alternative in most studies, this superiority does not hold against povidone–iodine plus alcohol as used in this study.

The primary limitation of the study is its retrospective nature. Propensity score adjustment is no substitute for a properly designed, randomised controlled trial (RCT). The retrospective nature of the study cannot account for the unknown variables affecting the outcome that are not correlated strongly with measured variables. However, retrospective comparisons with propensity score adjustment are more versatile and offer a useful way of interpreting large amounts of audit data and of seeking answers to questions that may present insuperable difficulties in the design of RCTs. Despite the retrospective and observational nature of the study, we provided data on a large cohort of exclusively 2% chlorhexidine gluconate and 70% isopropanol prepped patients undergoing cardiac surgery for comparison with 10% povidone–iodine in 30% industrial methylated spirit group, which has not been reported before, and demonstrated that 10% povidone–iodine in 30% industrial methylated spirit is as effective as 2% chlorhexidine gluconate in 70% isopropyl alcohol in reducing SSI after cardiac surgery with a marginal superiority in reducing organ-space infection.

Conclusion

In conclusion, our analysis confirms that that skin preparation in coronary artery bypass surgery with 10% povidone–iodine in 30% industrial methylated spirit reduces the incidence of organ-space infections with similar efficacy in preventing superficial and deep infections compared with 2% chlorhexidine gluconate in 70% isopropanol formulation. Our findings may be used in an economic assessment to identify financial savings without compromising patient safety. However, the results of this study need to be verified by a RCT.

Declaration of conflicting interests

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