

Original Article

Is there a difference between two different skin disinfection methods in cardiac surgery in terms of isolated pathogens?

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Abstract

Introduction: In this study, our aim was to prospectively compare the different methods of patient disinfections with scrubbing + iodine + alcohol, and the povidone iodine disinfection method, which can be described as classical, in terms of the pathogens isolated on skin and during early postoperative complications.

Methodology: Eighty patients undergoing cardiac surgery were included in the study. The patients were divided into two groups: group 1 (n = 48) patients who underwent scrub, iodine, followed by skin disinfection with alcohol, and group 2 (n = 32) who were treated with povidone iodine three times. The samples were immediately sent to the microbiology laboratory. Specimens from the wounds were incubated under aerobic and anaerobic conditions, and isolates were identified using standard microbiological techniques.

Results: In samples taken after disinfection in group 1, significantly less reproduction was observed compared to group 2 (p = 0.001). There was no difference in postoperative complications between the two groups except for pleural effusion (p = 0.040). *S. epidermidis* was the most frequently isolated pathogen in both groups.

Conclusion: We did not find a study which compares scrub + alcohol + iodine and povidone iodine in our literature review. We think that our study is original in this respect. We can conclude that skin disinfection with scrub + alcohol + iodine was superior to using only povidone iodine in terms of the pathogens isolated afterwards from the wound.

Key words: cardiac surgery; wound infection; povidone iodine; alcohol.

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Introduction

The incidence of postoperative sternal wound infection after open heart surgery is reported to range from 0.8-16%, but the average is 2% [1,2]. It is a rare complication that has a very high mortality [3]. The pathogens most often detected are *Staphylococcus aureus* and *S. epidermidis* species, which can be found as normal flora of the skin [4]. Hand hygiene, antibiotic prophylaxis, surgical technique and postoperative wound care have been reported to be effective for the prevention of sternum infection [5]. Perhaps the most important of these factors is pre-surgical skin hygiene and disinfection. The aim is to reduce the number of microorganisms on the skin before surgery, thus preventing subsequent infection. Solutions such as iodine, chlorhexidine, povidone iodine and scrub are already used for pre-surgical disinfection. In cardiac surgery, disinfection is achieved in multiple centers by cleaning the operation site with povidone iodine 3

times. In contrast, in our clinic, we use the gradual scrub-iodine-alcohol method for skin disinfection and we find very little wound infection or related complications. We could not find reports of studies on this subject in the literature, therefore, we aimed to compare the two different methods for skin disinfection in cardiac surgery in terms of the pathogens isolated and of early postoperative adverse events (first 30 days).

Methodology

Eighty patients undergoing cardiac surgery were included in the study. The patients were divided into two groups: group 1, (n = 48) patients who underwent scrub and iodine followed by skin disinfection with alcohol, and group 2, (n = 32) who were treated only with povidone iodine three times. Each patient was randomly assigned to group 1 or group 2. In both groups, microbiological swab samples were taken from the skin tissue on the sternum at different stages of

surgery. For group 1, the samples were taken twice, after staining with scrub + iodine + alcohol, and after the skin was closed at the end of the operation, each time from the skin tissue on the sternum. In group 2, the first sample was taken where skin was stained with povidone iodine three times before the operation, and the second sample was taken from the skin on the sternum at the end of the operation. The samples were immediately sent to the microbiology laboratory. Incubation of wound specimens was done under aerobic and anaerobic conditions, and identification of isolates was done using standard microbiological techniques. The two groups were compared in terms of pathogens isolated from the cultures and of adverse events including wound site infection that developed during the first 30 days post-surgery.

All patients underwent a detailed anamnesis and physical examination in the preoperative period. Routine measures were hemogram, urea, creatinine, alanine aminotransferase, aspartate aminotransferase, sodium, potassium, and C-reactive protein, as well as chest X-ray and ECG.

Patients with a history of iodine allergy, patients with infection at the operation site, patients undergoing redo cardiac surgery, and patients undergoing emergency surgery were excluded from the study. Hospital patient files and the hospital computer registry system was used to gather data. None of the patients in our study were bathed with povidone iodine or chlorhexidine before the surgery.

All steps were conducted in accordance with the Helsinki Declaration criteria. Informed consent forms were obtained from each patient.

Cardiac Surgery

The surgeons were randomized to operate in one or the other of the two groups.

On-pump Surgery

Patients were opened by median sternotomy under general anesthesia. Left internal mammary artery (LIMA) and saphenous vein grafts were prepared by the same team. Right internal mammary artery (RIMA) was not removed in any patient. Then, cannulation was performed with standard aorta-atrial two-stage cannula and cardiopulmonary bypass was started when ACT value reached 480 seconds; the patients were cooled to 28 °C. Myocardial protection was achieved with crystalloid cardioplegia repeated every 20 minutes. Cardioplegia was given antegrade at 20 minute intervals. First right coronary artery and/or posterior descending branch, then circumflex coronary artery

system, and finally left anterior descending coronary artery (LAD) and diagonal artery were bypassed. LIMA was preferred for LAD in all patients. Proximal anastomoses were performed to the ascending aorta under the side clamp. Cardiopulmonary bypass was terminated after considering the hemodynamic parameters. The sternum was closed according to the skin and subcutaneous anatomy.

Off-pump Surgery

Median sternotomy was performed under general anesthesia. The same surgical team prepared LIMA and saphenous vein grafts. RIMA was not removed in any patient. The heart and pericardium were suspended with sling sutures. Octopus III (Medtronic Inc, Minneapolis, MN, USA) was used to stabilize the anastomosis site. For distal anastomosis, an intracoronary shunt (Clearview intracoronary shunt, Medtronic Inc., USA) was placed after the arteriotomy. Anastomosis was first bypassed to the LAD artery, then to the diagonal artery, then to the right coronary artery and finally to the circumflex coronary artery. Proximal anastomoses were anastomosed to the ascending aorta.

Intensive care follow-up

The patients were kept in the intensive care unit for 1 or 2 days. ECG, invasive arterial pressure, temperature, saturation, urine output, tube drainage and blood gas were monitored. Routine prophylactic 3 g/day cefazolin (Mustafa Nevzat, Istanbul, Turkey) was administered. Antihypertensive, antiaggregant and antianginal drugs were adjusted according to the patient's hemodynamics.

Wound Infection Criteria for diagnosis

Descriptions of infections were allocated among three groups: 1) superficial tissue infection, 2) deep wound infection including muscle and fascia, 3) organ or bone tissues infection, also known as mediastinitis [6,7]. Localized swelling, erythema, discharge and sternal distance were the criteria for infection. Surgical site infections do not include diathermy burns or stitch abscesses.

Statistical Analyses

All statistical analyses were performed using R 3.6.0 (www.r-project.com). Student t-test or Mann-Whitney-U test were applied for continuous variables and Chi-square or Fisher Exact test for categorical data. The Kolmogorov-Smirnov test was used to determine whether the continuous variables fit the normal distribution before comparison. Categorical variables

data were summarized through counts (n) and percentages (%), Continuous variables were expressed as mean \pm standard deviation or median (interquartile range). A $p < 0.05$ was considered statistically significant.

Results

All disinfection regimens were well tolerated: none of the disinfection regimens resulted in skin irritation or allergic reactions. There was a statistically significant difference between the two groups among EuroSCORE, diabetes mellitus and chronic obstructive pulmonary disease patients ($p = 0.005, 0.021, 0.004$, respectively) (Table 1). There was no difference between preoperative CRP (mg/L) and leukocyte (K/ μ L) values. However, there was a difference between postoperative day 0 leukocyte (K/ μ L), postoperative day 0 CRP (mg/L) and postoperative 3rd day leukocyte (K/ μ L), postoperative 3rd day CRP (mg/L) respectively ($p = 0.001, < 0.001, 0.004, 0.016$)

Operative and postoperative data showed a difference between operation time (hours) and period of hospitalization (days) ($p < 0.001, < 0.001$, respectively) (Table 2).

In addition, what we consider the most important finding in our research is that the number of patients with reproduction in the swab culture was found to be less in group 1 compared to group 2 ($p = 0.001$). As a postoperative complication, only pleural effusion was found to differ between the two groups ($p = 0.040$). There were no other differences in terms of complications (Table 3).

The types of surgery performed for both groups are shown in detail in Table 4. One patient in group 1 underwent tubular graft interposition for type 1 aortic dissection and one patient in group 2 underwent tubular graft interposition due to ascending aortic aneurysm. In addition, 1 patient in group 1 underwent a Bentall operation for ascending aortic aneurysm (Table 4).

Table 1. Demographic differences between two treatment groups.

Demographic variables	Group 1	Group 2	p-value
EuroSCORE	3 (2 – 5)	1.5 (0 – 3)	0.005 [†]
Age (years)	62.31 \pm 10.65	58 \pm 11.54	0.090
Sex, n (%)			0.999
Male	35 (72.9)	23 (71.9)	
Female	13 (27.1)	9 (28.1)	
HT, n (%)			0.149
No	11 (22.9)	13 (40.6)	
Yes	37 (77.1)	19 (59.4)	
HL, n (%)			0.814
No	29 (60.4)	21 (65.6)	
Yes	19 (39.6)	11 (34.4)	
DM, n (%)			0.021 [#]
No	23 (47.9)	24 (75)	
Yes	25 (52.1)	8 (25)	
Preoperative left ventricular EF (%)	57 (48.75 – 60)	60 (40 – 60)	0.601
Smoking, n (%)			0.552
No	27 (56.2)	15 (46.9)	
Yes	21 (43.7)	17 (53.1)	
COPD, n (%)			0.004 [#]
No	38 (79.2)	32 (100)	
Yes	10 (20.8)	0 (0)	
CRF, n (%)			0.514
No	46 (95.8)	32 (100)	
Yes	2 (4.2)	0 (0)	
Peripheral artery patient, n (%)			0.646
No	45 (93.7)	31 (96.9)	
Yes	3 (6.2)	1 (3.1)	
Carotid stenosis, n (%)			0.400
No	48 (100)	31 (96.9)	
Yes	0 (0)	1 (3.1)	

Values were described as mean \pm standard deviation, median (interquartile range) or counts (n) and percentages (%), as appropriate; ns: not significant; $p < 0.05$ was considered statistically significant; [†] Mann Whitney-U test; [#] Chi Square or Fisher Exact test. Abbreviations: HT: hypertension; HL: hyperlipidemia; DM: diabetes mellitus; COPD: chronic obstructive pulmonary disease; CRF: chronic renal failure; EF: ejection fraction.

Table 2. Operative and postoperative data.

	Group 1	Group 2	p-value
Number of anastomoses	3.14 ± 1.27	3.07 ± 0.89	0.807
X-clemp (hrs)	51.04 ± 30.04	53.83 ± 24.20	0.677
CPB time (hrs)	99.11 ± 43.29	88.48 ± 32.24	0.261
Operation duration (hrs)	295.33 ± 41.92	175.78 ± 32.18	< 0.001 [†]
Off-pump technique, n (%)			0.982
No	42 (87.5)	28 (90.3)	
Yes	6 (12.5)	3 (9.7)	
Length of stay in the ICU (days)	2.27 ± 0.68	2.13 ± 0.42	0.238
Length of hospitalization (days)	8.81 ± 4.42	6.22 ± 1.01	< 0.001 [†]

Values were described as mean ± standard deviation or counts (n) and percentages (%), as appropriate; ns: not significant; p < 0.05 was considered statistically significant; [†] student t test. Abbreviations: hrs: hours; CPB: cardiopulmonary bypass; ICU: intensive care unit.

Table 3. Postoperative early adverse events.

	Group 1	Group 2	p-value
Reproduction group, n (%)			0.001 [#]
No	34 (70.8)	11 (34.4)	
Yes	14 (29.2)	21 (65.6)	
Discharge, n (%)			0.384
No	46 (95.8)	29 (90.6)	
Yes	2 (4.2)	3 (9.4)	
Sternal distance, n (%)			0.060
No	48 (100)	29 (90.6)	
Yes	0 (0)	3 (9.4)	
Mediastinitis, n (%)			
No	48 (100)	32 (100)	
Pleural effusion, n (%)			0.040 [#]
No	42 (87.5)	22 (68.8)	
Yes	6 (12.5)	10 (31.3)	
AF, n (%)			0.277
No	43 (89.6)	25 (78.1)	
Yes	5 (10.4)	7 (21.9)	
Lung infection, n (%)			0.514
No	46 (95.8)	32 (100)	
Yes	2 (4.2)	0 (0)	
Readmission, n (%)			0.999
No	46 (95.8)	31 (96.9)	
Yes	2 (4.2)	1 (3.1)	
Mortality, n (%)			0.999
No	47 (97.9)	32 (100)	
Yes	1 (2.1)	0 (0)	

Values were described as counts (n) and percentages (%), as appropriate; ns: not significant; p < 0.05 was considered statistically significant; [#] Chi-square test. Abbreviations: AF: atrial fibrillation.

Table 4. Types of operation.

Operation type	Group 1	Group 2
CABG	45	26
Off-pump	6	0
On-pump	39	26
MVR	0	3
AVR	1	0
AVR+MVR	0	2
Ascending aortic tubular graft implantation	1	1
Benthall operation	1	0
Total	48	32

CABG: Coronary artery bypass graft, MVR: Mitral valve replacement; AVR: Aorta valve replacement.

Reproductive pathogen types are shown in Table 5. We found that the same pathogen was produced in all stages or in some cases in one stage, regardless of the stage of growth in the group. Therefore, the stage of reproduction of the pathogen was not further considered.

Discussion

In reviewing the literature, we did not find a study which compares scrub + alcohol + iodine to povidone iodine. Our study is original in this respect. In addition, significantly less reproduction was observed in samples taken after disinfection in group 1 (scrub + iodine+ alcohol) compared to the group 2 (povidone iodine only) (p = 0.001). There was no difference in postoperative complications between the two groups except for pleural effusion (p = 0.040). *S. epidermidis* was the most frequently isolated pathogen in both groups.

Human skin and mucous membranes contain a complex and heterogeneous combination of microorganisms called the flora. The most important microorganisms of skin flora include coagulase negative staphylococci (CNS). A relationship has been reported between CNS and implantation of a foreign body (such as a heart valve or orthopedic prostheses) in the body [8]. This is an extremely important issue, because the effects of skin disinfection methods on the development of infection after surgery has been neglected by many people for years. The highest rate of CNS infections is with *S. epidermidis* [9-13].

To summarize the risk factors in surgical site infections: 1-Patient characteristics: patient's history of diabetes, smoking, steroid use, malnutrition, prolonged preoperative hospital stays, nasal preoperative colonization of *S. aureus*, perioperative transfusion. 2 - Operative factors: I-Preoperative: preoperative antiseptic shower or bath, shaving of the hair around the surgical site, preoperative preparation of the skin with antiseptic skin disinfectants containing chlorhexidine gluconate and povidone iodine in the incision area. II-Intraoperative Factors: ventilation, sterilization of surgical instruments, surgical clothing and drapes,

asepsis and surgical technique. III- Surgical feature : factors such as postoperative wound care and postoperative hospital stay are important [14]. Despite recent advances in perioperative care, surgical site infection remains an important problem in cardiac surgery due to increases in-hospital mortality and morbidity and in cost. Cardiac surgery has been found to increase the likelihood of developing sternal wound infection, due to the complex procedures involved [15].

The use of antibiotics in the prevention of wound infection in cardiac surgery is performed prophylactically, although the effectiveness of the cleaned operating room conditions is not known. Disinfection is the process of destroying or inactivating pathogenic organisms. Chemical disinfection is used for preoperative patients and various substances have been developed for this purpose. Iodine, first introduced by Bernard Courtois in 1811, is the oldest antiseptic substance and has been used to disinfect patients before surgical intervention for a long time [16]. However, because of its skin irritating properties and its coloring the skin to a very dark color, alternatives like aqueous or alcohol-dissolved preparations have been developed. An aqueous or alcoholic solution containing 10% iodine is known as povidone iodine. The 7.5% solution is called scrub. The main mechanism of action of iodine and its solutions in various ratios is that microorganisms penetrate cell membranes and break down proteins, nucleotides and fatty acids in the cytoplasmic membrane and cytoplasm. Due to its excellent penetration and poor reactivity with protein components (i-functions), iodine easily enters the skin where it forms a solid solution. Povidone iodine is a water soluble complex that is used to disinfect the surface of the skin. It has a long-term antiseptic effect against a broad spectrum of microbes such as gram-positive and gram-negative bacteria, including protozoa and yeasts [17]. One of the most important side effects may be thyroid dysfunction due to iodine overdose [18].

Another substance is chlorhexidine gluconate, which is used for both hand antiseptic and patient cleaning in recent years. The combination with chlorhexidine-alcohol has recently been studied

Table 5. Types of reproducing pathogens.

Reproducing pathogens	Group 1	Group 2
<i>S. epidermidis</i>	11	16
<i>S. aureus</i>	0	3
Non-hemolytic streptococci	0	1
Corynebacterium species	0	1
Diphtheroid bacillus	2	0
Total	13	21

intensively. It binds to the skin with high affinity, has high antibacterial activity and has longer residual effects. However, it is more expensive than many disinfectants and is associated with allergic reactions [19].

It is possible to come across studies comparing the substances used as disinfectants in literature for various surgeries. No matter how much the skin is cleansed, it is not possible to destroy the microorganisms on it. In skin disinfection, there is still no material or method that is recognized by everyone as ‘the best skin disinfectant’ or ‘best skin disinfection method’. Although there are studies comparing chlorhexidine and povidone iodine used as disinfectants, little is known about which might be superior. In a meta-analysis of 8 studies involving 5031 patients comparing chlorhexidine and povidone iodine, it was found that chlorhexidine was significantly superior in preventing postoperative surgical wound infection [20]. Darouiche *et al.* studied 849 patients, and reported that chlorhexidine – alcohol as a preoperative disinfectant was superior to povidone iodine alone in preventing surgical wound infection [21]. Preoperatively applying chlorhexidine – alcohol before Cesarean skin preparation does not decrease the frequency of surgical-site infection compared to povidone–iodine, according to a contemporary randomized controlled study on 932 patients [22]. In a single center study of 3209 patients undergoing general surgery, Swenson and colleagues investigated the application of iodine in aqueous solution with chlorhexidine–alcohol (ChlorPrep®; Cardinal Health, Dublin, Ohio, USA) and iodine–alcohol (DuraPrep™; 3M, Maplewood, Minnesota, USA). According to their results, surgical-site infection rates were respectively 6.4, 7.1 and 3.9 per cent., implying that iodine–alcohol was better for the prevention of surgical-site infection [23]. Again, in a recent systematic review, it was unclear which antiseptics are superior to others [24].

Another important point is that for the studies on chlorhexidine and povidone iodine, the effect of alcohol was ignored. However, alcohol is known to have a disinfectant effect on its own. In other words, it was seen that chlorhexidine-alcohol formulations showed differences in infection rates when compared to aqueous-based or alcohol-based iodine solutions [25]. Another proof of this statement is from a study by Raja *et al.* on 728 patients, where 10% povidone iodine and 30% industrial methyl alcohol solution were compared to 2% chlorhexidine gluconate in 70% isopropanol formulation as disinfectant in coronary artery bypass

surgery to prevent superficial and deep infections. The effects of the two were found to be similar [26].

However, we did not find any studies in the literature on whether there is a difference in reproduction in patients undergoing cardiac surgery, comparing those with iodine + alcohol solutions versus those with only water-based iodine solution. In addition, we did not find any association with postoperative complications in the literature. In our study, finding less bacterial growth in cultures from group 1 may have been due to a positive interaction of iodine-containing disinfectants with alcohol.

Conclusions

One of the most feared complications after open heart surgery is unexpectedly losing the patient after mediastinitis and infection at the wound site. Such complications are important because of their undesirable results such as mortality, morbidity, long hospital stay, and increased cost [7]. We set out to find an answer to how much of this could be prevented during the disinfection phase, which is the beginning of surgery. We prospectively compared the difference between scrub + iodine + alcohol, which is a different patient staining method to povidone iodine, the classical method for disinfection, in terms of pathogens isolated from the skin. There was a difference between the two methods in terms of reproduction in swab samples taken over the sternum. Using the different staining methods, which could be seen as a small detail, we found that the amount of pathogen produced in the sternal surgical field could be significantly reduced.

Limitations of the study

We could not fully determine the mechanism to explain the difference between the two treatment groups. Depending on the disinfectant effect of alcohol on its own or the difference in the absorption of iodine, reproduction may be different between the two groups. Despite it being a prospective study, the number of patients was small. Disinfectant products are often mixed with alcohol or water, which may make it difficult to draw general conclusions about the active ingredient. In our study, the fact that alcohol was used in only one group could be a confounding factor. Therefore, large, well conducted randomized controlled trials with consistent protocols comparing disinfectant agents in the same solution (water/alcohol) are needed. In addition, we did not compare iodine with chlorhexidine. Perhaps a study involving chlorhexidine could determine the most appropriate disinfection method in cardiac surgery. Another factor that was

missing in our study was the presence of nasal carriage in terms of preoperative staphylococci and no prophylaxis was performed.

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