The Heart Surgery Forum #2009-1162
13 (4), 2010 [Epub August 2010]
doi: 10.1532/HSF98.20091162

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Dermacyn® Irrigation in Reducing Infection of a Median Sternotomy Wound

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ABSTRACT

Background: Sternal wound infection is an infrequent yet potentially devastating complication following sternotomy. Among the standard practices used as preventive measures are the use of prophylactic antibiotics and povidone-iodine as an irrigation agent. A new antiseptic agent, Dermacyn® superoxidized water (Oculus Innovative Sciences), has recently been used as a wound-irrigation agent before the closure of sternotomy wounds.

Methods: This prospective, randomized clinical trial was conducted to compare the effectiveness of Dermacyn and povidone-iodine in reducing sternotomy wound infection in patients undergoing coronary artery bypass graft surgery. Upon chest closure and after insertion of sternal wires, wounds were soaked for 15 minutes with either Dermacyn or povidone-iodine. Subcutaneous tissue and skin were then closed routinely. Patients were followed up, and any wound infection was analyzed.

Results: Of the 178 patients, 88 patients were in the Dermacyn group, and 90 were in the povidone-iodine group. The mean (±SD) age of the patients was 61.1 ± 7.6 years. The incidence of sternotomy wound infection was 19 cases (10.7%). Five (5.7%) of these cases were from the Dermacyn group, and 14 (15.6%) were from the povidone-iodine group (P = .033). No Dermacyn-related complication was identified.

Conclusion: We found Dermacyn to be safe and more effective as a wound-irrigation agent than povidone-iodine for preventing sternotomy wound infection.

INTRODUCTION

Patients undergoing coronary artery bypass grafting (CABG) surgery are exposed to possible sternal wound infection despite the procedure being categorized as clean surgery. Infections range from superficial infection to deeper infection of soft tissue, sternal osteomyelitis, and mediastinitis. The incidence of such infections ranges from 0.9% to 20% of cases [Loop 1990; Ulicny 1991], and the incidence of mediastinitis reported in most studies is 1% to 2% [El Oakley 1996; Bitkover 1998]. Although deep sternal wound infections, including mediastinitis, are infrequent complications, such infections are associated with significant morbidity and mortality (between 9.8% and 14% [Loop 1990; Ulicny 1991; El Oakley 1996]), prolonged hospitalization, and an increased financial burden on the health care system [Vegas 1993]. Therefore, it is vital to prevent infection of the sternotomy wound following surgery. Among the standard practices for prevention are the prophylactic use of antibiotics and placement of the pericardial drains to facilitate drainage of blood and serous fluid. These practices have been shown to lower the rate of deep sternal infection [Blanchard 1995]. Agents that irrigate the dermal wound have also been used to facilitate removal of debris before wound closure. One common practice is the use of saline and antiseptics such as povidone-iodine as wound-irrigation agents.

Dermacyn® (Oculus Innovative Sciences, Petaluma, CA, USA), a superoxidized aqueous solution, is a new antiseptic agent cleared by the US Food and Drug Administration (FDA) that has recently been used in our center as an irrigation agent during closure of sternotomy wounds. The initial experience has been good with no adverse effects. Dermacyn is produced by means of a proprietary electrolysis process that uses a sophisticated, unique multichamber system. The solution is manufactured from purified water and sodium chloride. The electrolysis process separates and captures the ions to produce a sterile, pH-neutral solution consisting of a stable controlled formula of reactive oxygen and chlorine species [Oculus Innovative Sciences 2006]. The active compounds in Dermacyn are 99.9% water, hypochlorous acid, and sodium hypochlorite, and the inactive compounds are sodium carbonate, sodium hydroxide, hydrogen peroxide, chlorine dioxide, and ozone.

Dermacyn wound-irrigation agent is applied to chemically debride, flush, and cleanse the wound surface. The reactive oxygen species assist in promoting the body's own healing process by reducing the microbial load and via the agent's

Received October 13, 2009; received in revised form November 8, 2009; accepted November 24, 2009.

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moistening properties [Bongiovanni 2006]. Several studies have found Dermacyn to be safe and to exhibit a wide antimicrobial spectrum [Landa-Solis 2005]. Paola et al [2006] proved the effectiveness of Dermacyn over povidone-iodine and Dermacyn's safety in treating the infected diabetic foot. A study of another series by Ohno et al [2000] showed that superoxidized water had no adverse effect on hemodynamics and was safe when used as a mediastinal irrigation solution during open heart surgery. Dermacyn has also been subjected to a series of biocompatibility tests. These tests were performed in accordance with the requirements set forth by International Standards Organization and FDA guidelines. The product has also been tested in animal models to satisfy FDA requirements and to ensure its safety and efficacy [Oculus Innovative Sciences 2006]. Several studies, however, have identified various factors that contribute to wound infection that always need to be considered [Zacharias 1996].

We therefore conducted this study to compare the effectiveness of Dermacyn irrigation and povidone-iodine with respect to reducing the incidence of sternotomy wound infection following CABG. We also evaluated our study population to identify the potential risk factors for sternotomy wound infection following CABG.

MATERIALS AND METHODS

This prospective randomized clinical trial took place between June 2007 and December 2008. All patients scheduled for elective CABG were included in this trial. Exclusion criteria included emergency cases, patients who underwent other surgical procedures in addition to CABG, patients allergic to Dermacyn, and those who had infective or other skin lesions over anterior chest wall area. Informed consent was obtained, and patients were consecutively randomized into 2 groups. Group A patients used Dermacyn as a wound-irrigation agent, and group B patients used povidone-iodine. All patients received intravenous prophylaxis with 1.2 g Augmentin (amoxicillin and clavulanate) at induction. Before the surgery, the skin was cleaned with 10% povidone-iodine solution and covered with polyurethane drapes. CABG was performed through a standard median sternotomy by 3 cardiothoracic surgeons. Upon closure, bone wax and diathermy were used sparingly for hemostasis. Two drains were normally left in the mediastinal cavity. The sternum was closed primarily with no. 6 steel wires in a figure-of-eight manner. In both groups, the wounds were then soaked for 15 minutes after insertion of the sternal wires. The subcutaneous tissue was closed in 2 layers with polyglactin 1-0 suture, and the skin was closed subcuticularly with Vicryl 3-0 suture.

Diagnosis and Follow-up

The sternotomy wounds were inspected on postoperative day 2 and daily until discharge. Patients were then followed up at 2, 4, and 6 weeks postoperatively to assess for the presence of wound infection and Dermacyn side effects. The primary outcome was the presence of sternotomy wound infection, which was defined according to the Centers for Disease Control and Prevention in their National Nosocomial Infections System [Horan 1992]. Wound infections were graded according to Horan et al [1992] as superficial (involving the skin and subcutaneous tissue of the incision), deep (involving fascia, muscle layers, and sternum), or deep organ space. The nature of discharge from the wounds was documented, and samples of the discharge were sent for culture and sensitivity analyses. The risk factors for wound infections were identified and analyzed.

Table 1. Clinical Characteristics of the 178 Patients Involved in the Trial*

Age, *y*	61.1 ± 7.6
Male-female ratio	3.24:1
COPD, n	66 (37.1%)
Diabetes mellitus, n	79 (44.4%)
ESRF, n	32 (18.0%)
Obesity (BMI >30 kg/m^2), n	20 (11.2%)
Smoking, n	66 (37.1%)
On-pump/off-pump surgery, n	153 (86%)/25 (14%)
Bypass time, min	99.0 ± 7.4
IMA harvested, n	171 (96.1%)

*Data are presented as the mean ± SD where indicated. COPD indicates chronic obstructive pulmonary disease; ESRF, end-stage renal failure; BMI, body mass index; IMA, internal mammary artery.

Ethical Considerations

This trial involved no financial gain and was approved by the research and ethics committee of the Universiti Kebangsaan Malaysia Medical Centre (code no. FF-236-2007).

Statistical Analysis

Data were stored and analyzed with SPSS software (version 12.0; SPSS, Chicago, IL, USA). Continuous and categorical variables were analyzed with the independent Student t test and the chi-square test, respectively. With the use of 95% confidence intervals, a P value <.05 was considered statistically significant.

RESULTS

We recruited 190 patients for this trial, 95 patients in each group. Twelve patients, however, dropped out owing to postoperative mortality (4 cases, 2 deaths due to poor left ventricular function of <20% and 2 deaths due to cerebrovascular accident) and chest reopened for bleeding (8 cases), leaving 178 patients remaining in the study. Eighty-eight patients were in group A, and 90 were in group B. The mean (±SD) age of the patients was 61.1 ± 7.6 years. The male-female ratio was 3:1. Diabetes mellitus and chronic obstructive pulmonary disease (COPD) were the most common comorbidities (44.4% and 37.1%, respectively). End-stage renal failure (ESRF) and obesity were documented in 18% and 11.2% of cases, respectively. On-pump CABG surgery was performed in 86% of the patients with a mean cardiopulmonary bypass

Table 2. Comparison of Comorbidities and Intraoperative Details for the 2 Randomized Groups*

	Group A	Group B	*P*
Age, y	62.61 ± 7.7	59.54 ± 7.2	.085
COPD, n	35 (39.8%)	31 (34.4%)	.462
Diabetes mellitus, n	39 (44.3%)	40 (44.4%)	.986
ESRF, n	8 (9.1%)	24 (26.7%)	.002
Obesity (BMI >30 kg/m^2), n	7 (8.0 %)	13 (14.4%)	.170
Smoking, n	35 (39.8%)	31 (34.4%)	.462
On-pump surgery, n	73 (83%)	80 (88.9%)	.255
Bypass time, min	98.14 ± 9.8	99.83 ± 9.9	.076
IMA harvested, n	84 (95.5%)	87 (96.7%)	.677

*Data are presented as the mean ± SD where indicated. COPD indicates chronic obstructive pulmonary disease; ESRF, end-stage renal failure; BMI, body mass index; IMA, internal mammary artery.

time of 99 ± 7.4 minutes. A single internal mammary artery (IMA) was harvested in 171 patients (96.1%). Table 1 summarizes the patients' clinical characteristics. The 2 groups were well matched with respect to demographic, comorbidity, and intraoperative variables. The only exception was ESRF, which was more prevalent in group B (26.7%) than in group A (9.1%). Table 2 summarizes the comparison of comorbidities and intraoperative details of the 2 groups.

Sternal wound infections occurred in 19 patients (10.7%). Group B had a significantly higher incidence of infections (14 patients, 15.6%) than group A (5 patients, 5.7%) (*P* = .033, Table 3). All 5 patients who developed sternotomy wound infections in group A had superficial infections. Of the 14 patients in group B who developed infections, 10 had superficial infections, and the remaining 4 patients had deep sternal wound infections that led to sternal dehiscence requiring surgical debridement and repair (Table 4).

Bacteriology

Swabs for microbiology analyses were obtained from infected wounds. Of the 19 patients with infections, 11 patients had significant microbial growth. Six patients had *Staphylococcus aureus* infection, and *Acinobacter* sp was cultured in 2 patients. *Pseudomonas aeroginosa*, *Staphylococcus epidermidis*, and coagulase-negative *Staphylococcus* were isolated from 1 patient each.

Risk Factors

Risk factors were divided into preoperative, intraoperative, and postoperative factors. A univariate analysis of all preoperative variables revealed that COPD, diabetes mellitus, ESRF, obesity (body mass index >30 kg/m^2), and smoking were associated with an increased risk of sternal wound infection at a *P* level of <.05. In this study, however, age was not significantly associated with sternal wound infection. Intraoperatively, we studied 3 variables: the CABG technique, the use of an IMA, and bypass time. Bypass time was significantly associated with

Table 3. Incidence of Sternal Wound Infection in the 2 Groups*

	Sternal Wound		
	Infected	Not Infected	Total
Group A, n	5 (5.7%)	83 (94.3%)	88
Group B, n	14 (15.6%)	76 (84.4%)	90

*P = .033.

Table 4. Type of Infection

	Type of Infection		
	Superficial	Deep	Total
Group A, n	5 (100%)	0 (0%)	5
Group B, n	10 (71.4%)	4 (28.6%)	14

the risk of infection ($P < .001$). Patients who had an IMA harvested, however, were not associated with an increased risk of infection. The duration of mechanical ventilation and the length of intensive care unit (ICU) stay, which were studied as postoperative risk factors of sternotomy wound infection in this trial, were significantly associated with an increased risk of wound infection (Table 5).

DISCUSSION

It is imperative to reduce the risk of sternotomy wound infection, and many standard practices have been described, including meticulous scrubbing, skin preparation, use of disposable prefabricated drapes, use of prophylactic antibiotics, and placement of the pericardial drains to facilitate the drainage of blood and serous fluid. The standard practice of irrigating the wound before closure with either normal saline or povidone-iodine has long been used in most centers. The efficacy of Dermacyn for antiseptic wound irrigation during closure of the sternotomy wound following open heart surgery has yet to be proven, however. As an antiseptic solution, it exerts a wide range of antimicrobial activities [Landa-Solis 2005; Oculus Innovative Sciences 2006]. It can also be applied when chemically debriding and cleansing wound surfaces. The mechanism of action in eradicating various microorganisms is well documented [Landa-Solis 2005]. The active agents in Dermacyn consist of both chlorine and reactive oxygen ions. It is believed that the bactericidal action exhibited by Dermacyn is due to the combined effect of these species. The reactive oxygen species is also beneficial in the wound-healing process. Both ions are often referred to as free radicals. A number of different types of free radicals are also produced naturally by the body. Many free radicals provide significant health benefits, whereas free radicals produced by radiation can be destructive in nature. Conversely, Dermacyn ions and free radicals are biological and are not produced by radiation. Dermacyn technology has been tested in accordance with FDA requirements to ensure that such free radicals do not cause any harm.

Table 5. Univariate Analysis of Preoperative Risk Factors for Sternal Infection*

	Infected (n = 19)	Not Infected (n = 159)	*P*
Age, y	63.0 ± 7.5	60.8 ± 7.6	.257
COPD, n	11 (57.9%)	55 (34.6%)	.047
Diabetes mellitus, n	13 (68.7%)	66 (41.5%)	.026
ESRF, n	11 (57.9%)	21 (13.2%)	.000
Obesity, n	16 (84.2%)	4 (5.2%)	.000
Smoking, n	11 (57.9%)	55 (34.6%)	.047
Bypass time, min	108.05 ± 11.5	96.4 ± 7.9	.000
IMA harvest, n	17 (89.5%)	154 (96.9%)	.118
Ventilation duration, h	10.84 ± 6.1	4.21 ± 0.7	.000
Length of ICU stay, d	2.63 ± 0.76	2.06 ± 0.23	.000

*Data are presented as the mean ± SD where indicated. COPD indicates chronic obstructive pulmonary disease; ESRF, end-stage renal failure; IMA, internal mammary artery; ICU, intensive care unit.

Table 6. Infected Cases among ESRF and non-ESRF Patients*

	Infected		
	ESRF	Non-ESRF	Total
Group A, n	3 (60%)	2 (40%)	5
Group B, n	8 (57.1%)	6 (42.9%)	14

*Odds ratio, 1.1.

In this study, the 5 patients from the Dermacyn group with infected wounds had only superficial infections, and they required only a course of antibiotics and wound dressings to treat the infection and to promote wound healing. Four patients from the povidone-iodine group with wound infection, however, had associated deep wound infection and sternal dehiscence. These patients required surgical debridement and sternal rewiring. The remaining 10 patients had superficial infections and were successfully treated with antibiotics and wound dressings. Obviously, these findings indicate that the Dermacyn group not only had a lower infection rate but also had less severe infections than the povidone-iodine group.

Many studies have demonstrated that the development of sternotomy wound infection following CABG is multifactorial. Most authors have classified the risk factors into 3 groups: preoperative factors pertaining to the patient, such as advanced age and comorbidities; intraoperative factors, such as a prolonged duration of operation and the need for reoperation; and postoperative factors, such as the use of an intra-aortic balloon pump, massive blood transfusion, and prolonged mechanical ventilation [Oschner 1972].

In the present study, we assessed 11 variables as potential risk factors for sternotomy wound infection. A univariate analysis was performed to determine the associations between these risk factors and wound infection (Table 5). In contrast to the results of other studies, we found that age was not significantly associated with sternotomy wound infection ($P = .257$). This result was probably because most of our patients were younger than 65 years, whereas several studies have shown that older patients are at high risk of developing wound infection. Our analysis revealed that patients who had diabetes mellitus and were obese were more likely to develop sternotomy wound infection, a result that is concordant with other studies [Moulton 1996]. Cigarette smoking and COPD were also identified as significant risk factors for sternal wound infection following CABG. More than 60% of our patients with infection were smokers and had COPD. The latter is frequently associated with an increased risk of postoperative mediastinitis, probably because of frequent coughing, which may contribute to wound dehiscence and thereby facilitate bacterial migration into the mediastinum. Patients with COPD also experience respiratory infections more frequently and prolonged weaning from mechanical ventilation [Grossi 1991]. The details of the pathophysiology causing the infection in these patients are beyond the scope of this report.

In this trial, we were unable to match the 2 groups with respect to the number of ESRF patients. ESRF was more prevalent in group B. The overall incidence of sternal wound infection in ESRF patients was statistically significant ($P < .001$). Further analysis, however, revealed that 3 (60%) of the 5 patients in group A and 8 (57.1%) of the 14 patients in group B who developed infection had ESRF. The calculated odds ratio between these 2 groups was 1.1, implying that sternotomy wound infection is equally likely to occur in the 2 groups, regardless of the type of irrigation used (Table 6). We observed that 14 patients (82.4%) who developed wound infection had bypass times >110 minutes. This finding was supported by the statistical analysis, which showed bypass time to be significantly associated with the risk of sternal infection. This finding is similar to findings from most other studies, which showed a higher incidence of sepsis with longer bypass times [Loop 1990]. Many studies have linked the use of IMA grafts to a higher incidence of sternal infections [Hirotani 2002]. Of the 19 patients who developed sternotomy wound infection in the present study, 17 (89.5%) had a single IMA harvested. This incidence showed that this variable did not make a significant contribution to the risk of sternal infection. Decreased sternal perfusion has been hypothesized as a cause for an increased incidence of sternal infections following use of an IMA [Carrier 1992]. Sofer et al [1999] showed that after bilateral IMA dissection, sternal perfusion was reduced by a mean of 24% ± 6%. Four weeks postoperatively, sternal blood flow was still reduced by a mean of 2% ± 2%. This low sternal perfusion may lead to tissue necrosis, and hence to an impaired wound-healing process. We tried to avoid bilateral IMA use unless it was absolutely necessary. Our results also confirmed that prolonged mechanical ventilation and a longer ICU stay were significantly associated with wound infection. All of our patients were ventilated and observed postoperatively in the cardiac beds in the general ICU rather than in a dedicated cardiac ICU. The risk of infection is generally greater in the

general ICU. These patients not only are exposed to endogenous infection (ie, normal commensals) but also are prone to contract infections from exogenous sources, such as the staff, other patients, and visitors.

This trial had certain limitations. The number of participants in this study was relatively small because our center is not the main center for cardiothoracic surgery in this region; thus, the logistics allowed for only a limited number of operations. In addition, the variables for risk factors for sternotomy wound infections were limited to 11. Although all patients underwent their operations with the same cardiothoracic surgical teams, we were not able to appoint a dedicated surgeon for closure of sternotomy wounds. Some nonobjective factors that might also have influenced this study include the number of staff and medical students entering and exiting the theater during surgery. This trial, however, suggests that the use of Dermacyn as a wound-irrigation agent at closure of sternotomy following CABG reduced the incidence of wound infection, compared with povidone-iodine. There were no adverse side effects associated with the use of Dermacyn. Therefore, it can be used without hesitancy in view of its effectiveness and safety as a wound-irrigation agent.

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