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Comparative analysis of the antiseptic effectiveness of two commercially available skin disinfectants in cardiac surgery – a preliminary report

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Abstract

Introduction: Appropriate antisepsis of the chest skin is key for successful prophylaxis against incisional surgical site infections in cardiac surgery.

Aim of the study: Comparative analysis of the antiseptic effectiveness of two commercially available agents.

Material and methods: The study involved 91 consecutive patients at the mean age of 66.2 ±9.9 years who underwent elective cardiac surgery. In order to disinfect the chest skin, chlorhexidine (Hibitan) in 70% ethanol was used in group H (n = 46) and povidone-iodine (Braunoderm) in 50% propanol was used in group B (n = 45). The primary clinical endpoint was the occurrence of incisional surgical site infection (either deep or superficial) within the first 30 days after the elective surgery. Moreover, leukocyte counts (WBC) as well as C-reactive protein (CRP) and procalcitonin (PCT) concentrations were analyzed preoperatively and postoperatively – 24, 48, 72 hours, and 7 days after the operation. Additionally, peak values of the aforementioned laboratory parameters (WBC_{max}, CRP_{max} and PCT_{max}) were also estimated in the consecutive measurements.

Results: The primary study endpoint was reached by 4 (8.9%) group B and 2 (4.3%) group H patients. In a single case from group B, a deep surgical site infection affecting the sternum was revealed. The values of all hematological parameters increased markedly after the surgery and were significantly higher ($p < 0.05$) in group B as compared to group H (WBC_{max} 15.2 ±2.9 vs. 14.1 ±2.4; CRP_{max} 190.4 ±41.0 vs. 112.7 ±35.2 mg/l and PCT_{max} 1.92 ±0.81 vs. 0.95 ±0.34 µg/l, in groups B and H, respectively).

Conclusions: Our findings may indicate that chlorhexidine in 70% ethanol is a more effective surgical site antiseptic agent in cardiac surgery as compared to povidone-iodine in 50% propanol.

Key words: skin antisepsis, chlorhexidine, surgical site infection.

Streszczenie

Wstęp: Kluczowe znaczenie w zapobieganiu zakażeniom rany po operacjach serca ma właściwa dezynfekcja skóry klatki piersiowej.

Cel pracy: Porównawcza ocena skuteczności dwóch komercyjnie dostępnych roztworów do odkażania ran.

Materiał i metody: Badaniem objęto kolejnych 91 chorych w wieku 66,2 ±9,9 roku poddanych planowym operacjom serca. W grupie H (n = 46) stosowano 70-procentowy roztwór alkoholu etylowego z chlorheksydyną (Hibitanem), w grupie B (n = 45) 50% roztwór alkoholu propylowego z polimerem winylopirolidonu i jodyną (Braunodermem). Za twardy kliniczny punkt końcowy przyjęto infekcję rany pooperacyjnej (głęboką lub powierzchowną) w okresie do 30 dni po zabiegu. Porównywano liczbę leukocytów (WBC), stężenie białka C-reaktywnego (C-reactive protein – CRP) oraz prokalcytoniny (PCT) przed operacją, 24, 48, 72 godziny i 7 dni po operacji oraz maksymalne ich wartości (WBC_{max}, CRP_{max}, PCT_{max}) w kolejnych pomiarach.

Wyniki: Twardy punkt końcowy badania osiągnęły 4 osoby (8,9%) z grupy B i 2 (4,3%) z grupy H. W jednym przypadku stwierdzono głęboką infekcję z zajęciem mostka (w grupie B). Wartości wszystkich analizowanych parametrów hematologicznych wzrosły po operacji i były istotnie ($p < 0,05$) wyższe w grupie B niż w grupie H (WBC_{max} 15,2 ±2,9 *vs* 14,1 ±2,4; CRP_{max} 190,4 ±41,0 *vs* 112,7 ±35,2 mg/l i PCT_{max} 1,92 ±0,81 *vs* 0,95 ±0,34 µg/l, odpowiednio w grupie B i H).

Wnioski: Wyniki badania mogą wskazywać, że 70-procentowy roztwór alkoholu etylowego z chlorheksydyną skuteczniej zapobiega wczesnym zakażeniom rany po operacjach serca niż 50-procentowy roztwór alkoholu propylowego z polimerem winylopirolidonu i jodyną.

Słowa kluczowe: odkażanie skóry, chlorheksydyna, zakażenie rany chirurgicznej.

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Introduction

Surgical site infections (SSIs) in patients undergoing extensive operations, including cardiac surgery, constitute a serious clinical problem [1-3]. It is estimated that SSIs occur in about 5% of cases after clean operations, while this rate may increase even up to 30% in the group of clean-contaminated surgical wounds [4]. One of the most crucial purposes of the contemporary surgical safety procedures is to limit the occurrence of SSIs [5]. Nowadays, elderly patients, who often suffer from concomitant disorders considered as risk factors for delayed wound healing, such as atherosclerosis or insulin-treated diabetes, constitute a systematically growing group of individuals undergoing various elective procedures, including cardiac surgery [6]. Moreover, cardiac operations are usually long-lasting and invasive, and they entail extensive exposure of the chest organs [7]. The use of an extracorporeal circuit is usually associated with hypothermia, systemic inflammatory response syndrome (SIRS), and the necessity of blood product transfusions. All of the above may have a potential adverse impact on wound healing [8, 9]. All infections, particularly those involving the mediastinum, increase the length and costs of hospitalization [10]. The patient's skin is a major source of pathogens that may cause SSIs [11, 12]. Recently, special groups for infection control have been established in many hospitals. They develop optimal strategies to minimize the incidence of SSIs, such as antiseptic showers, antibiotic prophylaxis, or preoperative hair clipping [13, 14]. However, proper skin disinfection just before surgery still remains a key factor. Currently, many antiseptic agents are available for preoperative preparation of the incision site skin. The most common disinfectants are chlorhexidine gluconate, iodophors (e.g. povidone-iodine) and alcohol-based solutions.

The purpose of this work was to compare, in a randomized study, the antiseptic effectiveness of chlorhexidine-alcohol and povidone-iodine agents in the prevention of incisional SSIs after elective cardiac surgical procedures.

Material and methods

Patients

Our prospective, randomized clinical study involved 94 consecutive patients (22 women and 72 men) at the mean age of 66.2 ±9.9 years (ranging from 29 to 83) who underwent elective cardiac procedures carried out via median sternotomy between February and April 2011. Patients (a) with pre-existing infections (e.g. infective endocarditis) treated with antibiotics, (b) operated on emergently due to complications resulting from percutaneous interventions, (c) treated surgically for aortic aneurysms or acute dissections (due to more aggressive perioperative antibiotic prophylaxis), and (d) requiring prolonged (exceeding 72 hours) intubation and mechanical ventilation were excluded from the study. The patients were randomly allocated to two subgroups. In each subgroup a different antiseptic agent was used before incising the chest skin. Chlorhexidine in 70% ethanol (manufactured in the hospital pharmacy) was used in group H, while povidone-iodine in 50% propyl alcohol (Braunoderm, B. Braun Melsungen AG, Melsungen, Germany) was employed in group B. Preoperative demographic and clinical characteristics, with particular emphasis on risk factors for delayed wound healing, are listed in Table I.

Patients and surgical site preparation

All patients had a shower and a bath with chlorhexidine gluconate soap (Hydrex, Ecolab sp. z o.o., Kraków, Poland) on the day prior to surgery. This procedure was repeated two hours before the surgery. Next, hair was removed from the chest with clippers. The first dose of antibiotic prophylaxis (Tarfazolin, Polfa Tarchomin SA, Poland) was administered intravenously just after the transfer to the operating room. The skin at the incision site was disinfected twice with either chlorhexidine (Hibitan) in 70% alcohol (group H) or povidone-iodine in 50% isopropyl alcohol (Braunoderm) (group B). After the skin dried, surgical film was applied and the operation began.

Skin-to-skin, extracorporeal circulation (ECC) and aortic cross-clamping (ACC) times were calculated. Moreover, the length of the incision was measured and any problems with film adhesion to the skin adjacent to the incision site were noted. Accidentally exposed skin was disinfected again and additional film was applied.

Clinical study endpoints

The primary clinical endpoint was the occurrence of incisional SSI within the early postoperative period, defined as the first 30 days after the surgery. Definitions of incisional infections (superficial or deep) were adopted from the CDC (Centers for Disease Control and Prevention) Guidelines [4, 15]. Deep incisional SSI was diagnosed if the sternum and mediastinum were involved. Patients with such complications usually require a rethoracotomy with restabilization of the sternum accompanied by active irrigation drainage. Superficial incisional SSIs were defined as confined to the skin and subcutaneous tissue; such infections were usually treated with appropriate antibiotics. In some of the cases with superficial infections, negative pressure wound therapy

Tab. I. Basic demographic and clinical data of patients enrolled in the study

Variables	Group B (n = 45)	Group H (n = 46)	P value
Age (years)	70.2 ±7.3	62.2 ±10.6	**< 0.001***
Gender (M/F)	38/7	33/13	0.146
Obesity (BMI above 30), n (%)	4 (8.9)	3 (6.5)	0.676
Diabetes, n (%) treated with insulin, n (%)	7 (15.6) 2 (4.4)	9 (19.6) 3 (6.5)	0.620 0.667
Renal failure[a], n (%)	3 (6.5)	4 (8.7)	0.676
COPD n (%)	4 (8.9)	5 (10.9)	0.754

[a]If GFR was below 30; *statistically significant differences; BMI – body mass index; COPD – chronic obstructive pulmonary disease

(Genadyne A4, Genadyne Biotechnologies, Great Neck, NY, United States) was employed. The secondary clinical endpoints included fever episodes (shown by at least two measurements), the necessity of prolonged (exceeding 48 hours) antibiotic prophylaxis, the initiation of therapy with broad-spectrum antibiotics, or targeted against the pathogens grown in blood cultures and/or from the material collected from the wound. Moreover, the length of in-hospital stay was also analyzed.

Evaluated laboratory parameters

In all patients, white blood cell counts (WBC), C-reactive protein (CRP) and procalcitonin (PCT) concentrations were measured at the time of admission (WBC_0, CRP_0, PCT_0) as well as 1 ($WBC_{1\ h}$), 24 ($WBC_{24\ h}$, $CRP_{24\ h}$, $PCT_{24\ h}$), 48 ($WBC_{48\ h}$, $CRP_{48\ h}$, $PCT_{48\ h}$), 72 hours ($WBC_{72\ h}$) and 7 days (WBC_{7d}, CRP_{7d}, PCT_{7d}) after surgery. Additionally, the peak values of the aforementioned variables (WBC_{max}, CRP_{max}, PCT_{max}) were collected from the consecutive measurements and analyzed.

Statistical analysis

Firstly, continuous variables were checked for normality using the Shapiro-Wilk W test. Those with normal distribution ($p < 0.05$ in the W test) were expressed as a mean with standard deviation and compared using an unpaired Student's t-test. The differences between the remaining variables were analyzed by means of the Mann-Whitney U test. The variation of hematological parameters in groups B and H in relation to the time after surgery was estimated by ANOVA with the post-hoc Scheffe test. Categorical and nominal variables were compared by means of Fisher's exact test. *P* values < 0.05 were considered to be statistically significant. The statistical analysis was performed using Statistica 7.0 computer software (StatSoft, Tulsa, OK, United States).

Results

One female 76-year-old CABG (coronary artery bypass graft) patient allocated to group H died on the 3rd post-operative day due to low cardiac output syndrome, which, in spite of the use of an invasive heart support method (intra-aortic balloon pump), eventually led to multiorgan failure. Additionally, in two other individuals (one in group B and one in group H) a control post-operative chest X-ray revealed abnormalities that might have suggested local inflammation. All the aforementioned subjects were excluded from our study.

Intraoperative period

There were no statistically significant differences between the groups with regard to skin incision length, mean skin-to-skin, ECC, and ACC times, cardiac surgical procedure types, as well as the rate of procedures involving the extraction of at least one internal mammary. However, the detachment of surgical film in the vicinity of the incision site was observed more often in group B (40% in group B vs. 19.6% in group H; $p < 0.05$) (Table II).

Clinical findings

The primary clinical endpoint was reached by 4 individuals (8.9%) in group B and 2 (4.3%) in group H. Only in one case was the infection evaluated as deep (group B patient) and the chest had to be reopened. Moreover, in a single case from group B, a negative pressure system was used to support the healing of a superficial incisional SSI. In all subjects who developed SSIs, detachment of surgical foil was observed during the operation. Additionally, all of these patients had diagnosed insulin-treated diabetes and body mass index (BMI) exceeding 30.

Fever episodes were noted more frequently in group B (9 patients; 20.0%) than in group H (3 patients; 6.5%) ($p = 0.050$). Prolonged antibiotic therapy or the introduction of a new antibiotic took place more frequently in group B [10 subjects (22.2%) in group B vs. 3 subjects (6.5%) in group H, $p = 0.034$]. Oral antibiotics were continued after discharge in 4 group B (8.9%) patients and only in 1 group H (2.2%) patient.

Group B subjects stayed in the hospital (10.7 ±2.6 days) markedly longer than group H patients (8.2 ±2.3 days) ($p = 0.004$).

Biochemical parameters

Preoperative values of the hematological parameters related to inflammatory response (WBC_0, CRP_0 and PCT_0) did not differ between the examined groups (Table III). After surgery, the values of all the aforementioned variables increased significantly to reach their peak either 24 hours (WBC, PCT in group H) or 48 hours (CRP, PCT in group B)

Tab. II. Intraoperative data

Variables[a]	Group B ($n = 45$)	Group H ($n = 46$)	*P* value
Skin incision length (cm)	26.5 ±4.1	26.2 ±2.4	0.728
Skin-to-skin time (min)	168.7 ±40.5	161.7 ±38.0	0.372
Operations in ECC OPCAB	22 (48.9%) 23 (51.1%)	21 (45.7%) 25 (54.3%)	0.760
ECC time (min)	68.4 ±15.1	69.5 ±17.9	0.829
ACC time (min)	48.8 ±13.7	49.0 ±15.7	0.953
Surgery type:			
Isolated CABG	37 (82.2%)	34 (73.9%)	0.239
Isolated valvular	6 (13.3%)	7 (15.2%)	0.799
Combined procedures[b]	2 (4.4%)	4 (8.7%)	0.418
Others	0	1 (2.2%)[c]	0.327
LIMA	37 (82.2%)	36 (78.3%)	0.239
LIMA + RIMA	2 (4.4%)	3 (6.5%)	0.667
Film detachment	18 (40.0%)	9 (19.6%)	**0.039***

[a]Continuous variables are expressed as mean ± standard deviation, categorical variables as number (n) and percent (%); [b]Combined procedures were defined as CABG concomitant with a procedure involving at least one cardiac valve (replacement or repair) or double-valved procedures; [c]Operation for left atrial myxoma; *statistically significant difference; ACC – aortic cross clamping time; ECC – extracorporeal circulation time; CABG – coronary artery bypass grafting; LIMA – left internal mammary artery; OPCAB – off-pump coronary artery bypass grafting; RIMA – right internal mammary artery

Tab. III. Results of selected biochemical parameters

Parameter mean ± standard deviation	Group B (n = 45)	Group H (n = 46)	P value
WBC_0 (× 10^9/l)	7.23 ±1.64	7.52 ±2.01	0.450
WBC_{max} (× 10^9/l)	15.2 ±2.9	14.1 ±2.4	**0.037***
CRP_0 (mg/l)	2.65 ±1.22	2.72 ±1.34	0.329
CRP_{max} (mg/l)	190.4 ±41.0	112.7 ±35.2	**0.033***
PCT_0 (µg/l)	0.03 ±0.01	0.02 0.01	0.265
PCT_{max} (µg/l)	1.92 ±0.81	0.95 ±0.34	**0.027***

*statistically significant difference; CRP – C-reactive protein; PCT – procalcitonin; WBC – white blood cell count

after surgery. The increase in hematological inflammatory markers was more pronounced in group B, as compared to group H. These findings are demonstrated in detail in Table III and presented graphically in Fig. 1. Moreover, the calculated WBC_{max}, CRP_{max}, and PCT_{max} were significantly higher in group B than in group H (Table III).

Discussion

In our study, we found that fewer patients had fever episodes and less frequently required non-standard antibiotic management when the chlorhexidine-alcohol agent was used during the antisepsis of the surgical site. Although twice as many patients in group B reached the clinical endpoint, as compared to group H, the statistical analysis did not reveal any significant differences between the studied subjects with respect to the incidence of incisional SSIs in the early postoperative period. It is likely that the results were influenced by the relatively small number of patients recruited for the study and the exceptionally low incidence of infectious postoperative complications. However, the higher values of inflammatory status parameters may constitute a reasonable rationale to consider the antiseptic agent used in group H as more effective in SSI prophylaxis.

The overall incidence of infections observed in our study (6.6%) did not differ from the findings reported previously [6, 16, 17]. However, it needs to be noted that our analysis involved chest incisional SSIs only. We did not take into account the delayed healing of lower extremity wounds in coronary artery bypass patients or organ infections. Additionally, the actual number of incisional infections may have been underestimated as only the first 30 postoperative days were evaluated. For example, Junkers *et al.* found that even up to 30% of such infections may occur after discharge between the 30th and 90th day after the operation [18]. On the other hand, Swenne *et al.* published the results of a study in which approximately 95% of sternal infections were observed in the early postoperative period of up to 30 days after surgery [19]. Moreover, we enrolled in our study not only patients undergoing coronary artery bypass grafting, but also patients undergoing valvular or combined procedures. The rate of adverse infectious events following valvular procedures may be higher because they require connecting the patient to a cardiopulmonary bypass circuit and usually entail at least moderate

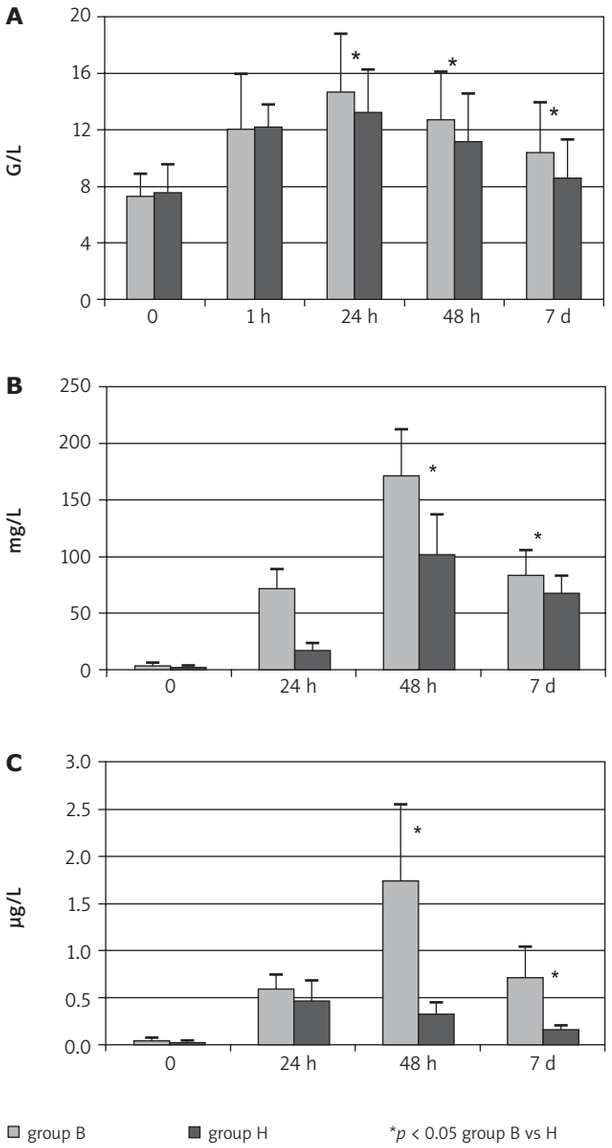

Fig. 1. Variability of the analyzed hematological parameters such as WBC (A), CRP (B) and PCT (C) in the early perioperative period

hypothermia; these are all considered to be potential risk factors for delayed wound healing [9].

Our findings support the earlier clinical reports stating that chlorhexidine-alcohol is more effective than iodine-based agents in SSI prophylaxis [20]. In the past, alcohol solutions of chlorhexidine were often compared to aquatic iodine agents [20]. Replacing the solvent with alcohol in the latter significantly improved its effectiveness [21]. Such an agent was also used in group B of our study. The differences in the effectiveness of these two antiseptic agents cannot be treated as the consequences of improper patient selection, because the patients did not differ from each other with respect to the independent risk factors of delayed wound healing, such as insulin-treated diabetes, obesity, and chronic obstructive pulmonary disease [16, 17]. Moreo-

ver, such intraoperative variables as skin-to-skin time, ACC time (corresponding to the period of hypothermia) or ECC time, as well as the rate of internal mammary harvesting (an important source of sternal perfusion), did not differ between the examined groups. The agents used for surgical site antisepsis feature a comparable spectrum of cidal activity. Moreover, the surgical film used in all patients had the same manufacturer and lot number. One possible explanation for the noted differences between the examined subjects may be the physical properties of the solutions, including their ability to dehydrate tissue, which may influence the adhesion of the film to the skin. The importance of this fact is that in all patients with incisional SSIs (deep and superficial), the surgical film detached from the patients' skin close to the site of the surgical access.

We are aware of the limitations of our study, such as the relatively small number of participants and the inclusion of patients with incisional SSIs only. This restricted the possibility of performing a more reliable statistical comparative analysis of patients with proper vs. improper film attachment within each subgroup of the study. The authors plan to continue this study and enroll more participants, which would allow for more precise conclusions regarding the optimal agents for SSI antisepsis in cardiac surgery.

Conclusions

Despite the fact that this prospective randomized one-center study was carried out on a relatively small number of patients, its results indicate that chlorhexidine-alcohol is more effective than alcohol-povidone-iodine in the prevention of incisional surgical site infections after elective cardiac surgical procedures.

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