Comparative study of two antimicrobial dressings in infected leg ulcers: a pilot study

• **Objective:** The aim of the study was to compare the efficacy of a microorganism-binding (MB) dressing with a silver-containing hydrofiber (SCH) dressing in controlling the bacterial loads of heavily colonised or locally infected chronic venous leg ulcers, before surgical management with homologous skin grafts.

• **Method:** A randomised comparative single centre study recruited patients presenting with hard-to-heal critically colonised or locally infected leg ulcers, who could be treated with skin grafting. Inclusion criteria included; ulcers of vascular aetiology, over 18 years old, a wound duration ≥6 months and ankle brachial index (ABPI) >0.6. Patients were randomly assigned to treatment with SCH dressings (Aquacel Ag) or MB dressing (Cutimed Sorbact). Dressings were changed daily over a four-day observation period, after which they were taken for a skin grafting procedure. Swab samples from ulcer beds were taken in order to quantify the bacterial load at inclusion (D0) and at the end of the observation period day 4 (D4). No antibiotics were administered before or during the evaluation period.

• **Results:** Both groups (n=20 SCH, n=20 MB) were similar in gender, age, pathophysiology (both had 15 patients with venous leg ulcers and 5 with arterial leg ulcers), ulcer surface, ulcer duration, treatment-related pain and initial bacterial load. Analysing bacterial load variation showed a significant reduction of bacterial burden at D4 in both groups. In the SCH group, we found an average bacterial load reduction of 41.6%, with an average reduction of 73.1% in the MB group ($p< 0.00001$). No serious adverse events were reported.

• **Conclusion:** Our evaluation confirmed that MB and SCH dressings are effective in reducing the bacterial burden in critically colonised or locally infected chronic leg ulcers, without inducing adverse events, with MB dressings significantly more effective.

• **Declaration of interest:** There were no external sources of funding for this study. The authors have no conflicts of interest to declare.

leg ulcers; infection; bacterial load; antimicrobial dressing; efficacy; skin allograft

Skin grafting failure due to infection was proposed in 1951 by Jackson.[1] In 1967 Krizek et al. published data showing that on average 94% of grafts survived when ≤10^5CFU/g were present in the tissue biopsies, whereas 19% survived when count exceeded 10^5CFU/g.[2] Another study[3] demonstrated the presence of *Pseudomona aeruginosa* and *Staphylococcus aureus* results in a significant probability of the skin graft failing to take. These finding were supported by Hogsberg et al.,[4] who concluded that a successful skin graft 'take' is less likely to occur with wounds containing more than 10^5 viable bacteria per gram of tissue.

Bacteria can secrete a large number of enzymes such as hyaluronidase, fibrinolysins, and proteases. In the case of skin grafting, these may damage the growth of capillaries through the fibrin layer between the granulation tissue and the graft.

Critical colonisation is used to describe the level of bacteria that inhibits wound healing but does not display classical signs of infections.[5] The term, which has been part of the wound care vocabulary for a long time, is frequently challenged[6] but not yet disproved. Synonyms for critical colonisation include: silent infection, covert infection, occult infection, refractory wound, subclinical infection, indolent wound, stunned wound, subacute infection and recalcitrant wound.[5] This means that clinical criteria are required to diagnose concealed infection.

Robson et al.[7] defined infection as a level of >10^5 microorganisms/g of tissue, and using quantitative bacteriology, they found that wounds undergoing delayed closure with <10 CFU/g healed successfully, while those with >10^5CFU/g did not.

For ulcers with high bacterial loads, the correct choice of a dressing to reduce bioburden is important. Adequate delivery of bactericidal agents to an infected ulcer can be very difficult; the dressing must be able to effectively decrease the microorganism population (planktonic and biofilms), with a broad spectrum of action. The dressing must not be toxic or induce resistance. It is widely accepted that topical antibiotics should be avoided owing to the risk of increasing bacterial resistance and contact dermatitis.[8]

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Dialkylcarbamoyl chloride-impregnated dressing for the prevention of surgical site infection in women undergoing cesarean section: a pilot study

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Abstract

Introduction: Incisional surgical site infections (SSIs) occur in approximately 1.8–9.2% of patients undergoing cesarean section (CS) and contribute to prolonged hospitalization time and increased treatment costs. Dressings impregnated with dialkylcarbamoyl chloride (DACC) are an innovative approach to wound treatment based on a solely physical mechanism of action, and therefore can be used safely and without time restrictions in women during the puerperal and lactation period.

Material and methods: A single-blinded randomized, controlled pilot study was conducted at the Mazovian Bródno Hospital, a tertiary care hospital, between December 2013 and March 2014, and it evaluated the presence of superficial and deep SSIs in patients during the first 14 days after a CS. Patients were randomly allocated to receive treatment with either a DACC dressing or a standard surgical dressing.

Results: One hundred and forty-two patients after planned or emergency CS were enrolled in the study. No significant differences between the groups were observed with regard to patients' basic demographic and perioperative characteristics. The rate of superficial and deep SSIs was 2.8% in the group of patients who received a DACC dressing compared to 9.8% in the group with a standard surgical dressing (p = 0.08). Patients with SSIs who received a standard surgical dressing required systemic antibiotic therapy significantly more frequently (p = 0.03). Based on the logistic regression model developed, the pre-pregnancy body mass index was the only statistically significant risk factor for SSI (p = 0.015).

Conclusions: The results of the pilot study indicate a decreasing tendency of the SSI rate in patients after a CS who received DACC impregnated dressings.

Key words: dialkylcarbamoyl chloride, surgical site infection, cesarean section.

Introduction

A rapid increase in the rate of cesarean sections (CS) observed within the last 30 years, especially in developed countries, has resulted in the fact that currently it is one of the most frequently performed surgical procedures. According to the literature data and depending on the region of the world, 0.4–40.5% of all deliveries have a surgical outcome [1]. Incisional wound infection defined according to the Centers for Disease Control and Prevention (CDC) criteria as a superficial or deep surgical site

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Original Articles

Randomized Controlled Trial Evaluating Dialkylcarbamoyl Chloride Impregnated Dressings for the Prevention of Surgical Site Infections in Adult Women Undergoing Cesarean Section

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Abstract

Background: Surgical site infections (SSI) occur in 1.8%–9.2% of women undergoing cesarean section (CS) and lead to greater morbidity rates and increased treatment costs. The aim of the study was to evaluate the efficacy and cost-effectiveness of dialkylcarbamoyl chloride (DACC) impregnated dressings to prevent SSI in women subject to CS.
Methods: Randomized, controlled trial was conducted at the Mazovian Bródno Hospital, a tertiary care center performing approximately 1300 deliveries per year, between June 2014 and April 2015. Patients were randomly allocated to receive either DACC impregnated dressing or standard surgical dressing (SSD) following skin closure. In order to analyze cost-effectiveness of the selected dressings in the group of patients who developed SSI, the costs of ambulatory visits, additional hospitalization, nursing care, and systemic antibiotic therapy were assessed. Independent risk factors for SSI were determined by multivariable logistic regression.
Results: Five hundred and forty-three women undergoing elective or emergency CS were enrolled. The SSI rates in the DACC and SSD groups were 1.8% and 5.2%, respectively ($p = 0.04$). The total cost of SSI prophylaxis and treatment was greater in the control group as compared with the study group (5775 EUR vs. 1065 EUR, respectively). Independent risk factors for SSI included higher pre-pregnancy body mass index (adjusted odds ratio [aOR] = 1.08; [95% confidence interval [CI]: 1.0–1.2]; $p < 0.05$), smoking in pregnancy (aOR = 5.34; [95% CI: 1.6–15.4]; $p < 0.01$), and SSD application (aOR = 2.94; [95% CI: 1.1–9.3]; $p < 0.05$).
Conclusion: The study confirmed the efficacy and cost-effectiveness of DACC impregnated dressings in SSI prevention among women undergoing CS.

Cesarean section (CS) remains to be one of the most common surgical procedures performed worldwide and available data indicate that surgical interventions constitute approximately 0.4%–40.5% of all deliveries [1]. Depending on the definition and the observational period, surgical site infection (SSI) occurs in about 1.8%–9.8% of all CS patients and leads to greater morbidity rates, prolonged hospitalization, and increased number of hospital readmissions [2–9]. Post-cesarean SSI has been estimated to extend the period of hospitalization by 4 d, and at the same time generating an additional cost of 3716 EUR per patient [9].

A recently published pilot study revealed a downward trend in SSI rates after CS if dialkylcarbamoyl chloride (DACC) impregnated dressings were used as method of post-operative SSI prevention [10]. The characteristic feature of the dressing, whose fibers were covered with a hydrophobic derivate of fatty acids, is its solely physical mechanism of action. It uses the interaction between hydrophobic molecules in the presence of aqueous medium, as well as the fact that the majority of pathogens responsible for the development of SSIs demonstrate moderate to high cell surface hydrophobicity (CSH) [11]. High CSH allows microorganism

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to adhere to cells and to initiate infection, at the same time causing their aggregation on the surface of the impregnated dressing, decreasing both their number in the wound bed and proliferation [12–16]. Described mechanism of action is not associated with the release of additional antimicrobial substances, thus eliminating the risk of cytotoxicity and sensitization, which is particularly important during the periods of puerperium and lactation [16]. To date, the efficacy of DACC-impregnated dressings has been proven in the treatment of venous, arterial and pressure ulcers, burns, diabetic foot, and hard-to-heal post-traumatic and post-operative surgical incisions [17–20].

Taking into consideration the steadily growing CS rates, as well as factors that are responsible for impaired wound healing in women of reproductive age, such as obesity, diabetes mellitus, or smoking, it is vital to search for new, efficient, and safe strategies of preventing obstetric SSI. Also, from the point of view of healthcare system economics, it is important to avoid additional costs, which would allow for a widespread application rather than in high-risk patients only. Therefore, the aim of the study was to evaluate the efficacy and cost-effectiveness of DACC impregnated dressings in the prevention of post-operative SSI among CS women.

Patients and Methods

Setting and study population

The single-blinded, randomized, controlled clinical study was conducted between June 2014 and April 2015 at the Mazovian Bródno Hospital, a tertiary referral center and a clinical hospital of the Medical University of Warsaw. Local Ethics Committee approved of the study (reference no. KB/127/2014 received on June 10, 2014) and written informed consent was obtained from all participants. The trial was registered with ClinicalTrials.gov (reference no. NCT02168023).

The inclusion criteria were: Patient age >18 y, emergency or elective CS, singleton or multiple pregnancy, mental and physical capacity to consent to participation in a clinical trial, CS performed by transverse skin incision followed by a transverse uterine incision in its lower segment, antibiotic prophylaxis administered zero to 30 min before the surgery, and wound irrigation with octenidine solution before subcutaneous tissue closure.

The patients were randomly assigned to two groups, depending on the applied dressing. Patients with DACC impregnated dressing (Sorbact Surgical Dressing®, ABIGO Medical AB, Sweden) constituted the study group, whereas women with standard surgical dressing (SSD) (Tegaderm + Pad®, 3M Health Care, St. Paul, MN) were recruited as control groups. Simple randomization with the 1:1 allocation ratio, conducted by an operating room (OR) nurse, was used to alternate the patients; even number: DACC dressing, and odd number: SSD. For masking purposes, all dressings were placed in white envelopes and sealed. The surgical team was blinded to the type of dressing until skin closure.

Data on patient demographics, peri- and post-operative course were collected from hospital medical records. Demographic parameters included: Age, race, pre-pregnancy weight, weight gain during pregnancy, height, pre-pregnancy body mass index (BMI), parity, gestational age; presence of diabetes mellitus (pre-gestational or gestational diabetes), hypertension (chronic hypertension or pregnancy-induced hypertension); smoking in pregnancy, history of previous CS, and presence of singleton/multiple pregnancy.

Peri- and post-operative parameters included: Type of dressing; mode of CS (emergency, elective); duration of the surgery; surgeon experience (resident, assistant specialist, consultant); type of anesthesia (spinal, general); presence of meconium stained amniotic fluid (MSAF); hemoglobin concentration 24 h before and 24 h after the surgery; receipt of blood transfusion, and length of post-operative hospital stay.

SSI-related parameters included: Presence of superficial or deep SSI during the first 14 d after the surgery, wound dehiscence; onset of the first symptoms of SSI; the need for systemic antibiotic therapy, hospital re-admission and/or re-operation; the number of ambulatory visits; length of additional hospitalization, and identification of the pathogen responsible for SSI.

The technique of a transverse skin incision (Pfannenstiel) followed by a transverse uterine incision in its lower segment was used in all women, as described previously [10]. For subcutaneous tissue and skin incision closure, single monofilament absorbable suture (Monosyn 2/0, B. Braun Melsungen AG, Germany) and subcuticular continuous monofilament non-absorbable suture (Prolene 2-0, Ethicon, Somerville, NJ), were used respectively. All patients received antibiotic prophylaxis (1g of cefazolin) administered zero to 30 min before the surgery according to Polish National Consultants of General Surgery and Clinical Microbiology recommendations and wound irrigation with octenidine solution (Octenisept®, Schülke & Mayr GmbH, Germany) proceeded subcutaneous tissue closure [21]. Octenidine is a cationic, surface active, topical antimicrobial agent with high bactericidal and fungicidal activity, and cytotoxicity similar to that of other common antiseptics such as chlorhexidine [22].

The study plan resembled the one described in the pilot study [10]. Briefly, the dressing was left in situ for the first 48 h post-operatively in all participants, unless there were reasons for replacement, e.g., wound hemorrhage or detachment of the dressing. After that time, the dressing was removed and the first clinical assessment of wound healing was performed. The patients were discharged home on post-operative day three, unless contraindicated, and recommended to revisit on day seven for skin suture removal and second wound evaluation. Third and final wound assessment was scheduled for post-operative day 14. Patients who failed to report for follow-up visits were excluded from the final analysis. Each wound assessment during patient hospitalization, the follow-up visits, or in case of patient's self-referral to an ambulatory center, was performed by one of two authors (PS, MB), blinded to the type of the dressing used.

Study outcome definitions

The symptoms of superficial or deep SSI were analyzed according to the U.S. Centers for Disease Control and Prevention (CDC) criteria [23]. Wound dehiscence was defined as separation of the skin, subcutaneous tissue, or fascia, resulting from infection. Time of primary hospitalization was defined as period from the day of surgery (day zero) to discharge from the hospital. Time of additional hospitalization

was defined as period from the first SSI symptoms to treatment completion and discharge from the hospital (in cases when SSI developed during primary hospitalization and was the main reason for prolonged stay in the hospital), or from day one of re-admission because of SSI until treatment completion and discharge from the hospital (in cases when primary hospitalization was finished). Emergency CS was defined as procedure performed within 30 min of the decision. Surgeon experience was determined on the bases of specialization in obstetrics and years of experience: Resident—physician in specialist training, assistant specialist—specialization in obstetrics for ≤5, consultant—specialization in obstetrics for >5 y.

Cost data analysis and definitions

In case of SSI occurrence, the following costs were analyzed: Systemic antibiotic therapy, ambulatory visits, additional hospitalization, and additional nursing care. The costs were calculated in Polish zloty (PLN) and then converted to Euro (EUR), based on the Polish National Bank exchange rate from June 1, 2015 (1 EUR = 4.1 PLN).

The cost of antibiotic therapy, defined as the cost of therapy from day one to the last day of SSI treatment, was calculated on the basis of antibiotic prices from the central hospital pharmacy and according to the manufacturer's specifications. The cost of ambulatory visit was calculated on the basis of classifying the patients into one of the Diagnosis Related Groups of Polish National Health Fund (DRG: W40), based on the diagnosis from the International Statistical Classification of Diseases and Related Health Problems v.10 (ICD-10-CM; o86.0—infection of obstetric surgical wound; o90.0—disruption of cesarean delivery wound), and the performed procedure, in accordance with the International Classification System for Surgical, Diagnostic and Therapeutic Procedures v.5.22 (ICD-9-CM; 86.28—non-excisional debridement of wound, infection or burn; 93.57—application of another wound dressing). Using the abovementioned data, the cost of a single ambulatory visit was estimated at 54 PLN (13 EUR). The costs of additional hospitalization in SSI patients who required prolonged primary hospitalization or readmission, together with the costs of additional nursing care obtained from the hospital financial office, amounted to 316 PLN (77 EUR) and 173 PLN (42 EUR) per day, respectively.

In order to determine the total costs of prophylaxis and treatment of SSI in both groups, the costs mentioned above were supplemented with the costs of dressings based on mean retail prices: DACC 11.5 PLN (2.8 EUR) and SSD 20 PLN (4.9 EUR).

Statistical analysis

Statistical analysis was performed using the R package v. 3.0.1 (The R Foundation for Statistical Computing, Vienna, Austria). Continuous variables were compared using the Mann-Whitney *U* test. For categorical variables, the χ^2 test or the Fisher exact test were applied. The p-value of <0.05 was considered as statistically significant.

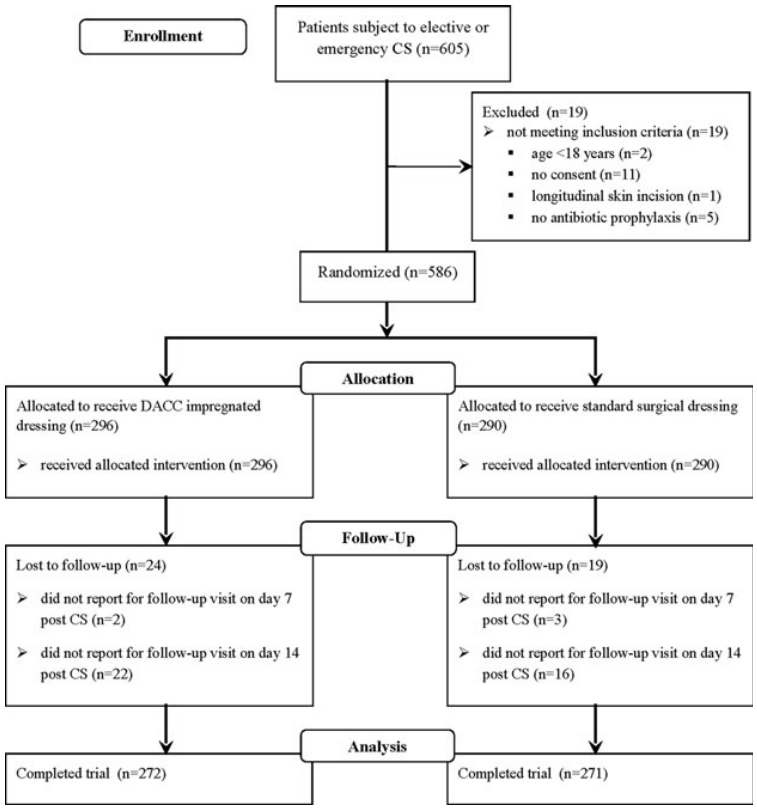

FIG. 1. CONSORT 2010 flow diagram of the recruitment process and randomization. CS, cesarean section; DACC, dialkylcarbamoyl chloride

Table 1. Characteristics of Patients Who Underwent Cesarean Section during the Study Period from June 2014 to April 2015

	Study group (n = *272*)	*Control group* (n = *271*)	*p*
Age (y)	31.2 ± 4.8 (18 – 43)	30.6 ± 4.8 (18 – 44)	.08
≤20	5 (1.8%)	4 (1.5%)	.63
21–30	114 (42.0%)	126 (46.5%)	
31–40	148 (54.4%)	134 (49.4%)	
>40	5 (1.8%)	7 (2.6%)	
Race			
Caucasian	269 (98.9%)	268 (98.9%)	>.999
Non-Caucasian	3 (1.1%)	3 (1.1%)	
Pre-pregnancy weight (kg)	65.8 ± 13.2 (40 –138)	66.4 ± 14.6 (39 –129)	.69
Weight gain during pregnancy (kg)	14.3 ± 6.0 (0 – 40)	14.4 ± 5.6 (0 – 38)	.64
Height (m)	1.66 ± 0.06 (1.48– 1.81)	1.65 ± 0.06 (1.4 – 1.84)	.55
Pre-pregnancy BMI (kg/m^2)	23.9 ± 4.5 (16.3 – 47.7)	24.2 ± 4.9 (14.5 – 43.6)	.57
BMI <25	193 (70.9%)	176 (64.9%)	.31
BMI ≥25 and <30	53 (19.5%)	62 (22.9%)	
BMI ≥30	26 (9.6%)	33 (12.2%)	
Parity			
Primiparous	131 (48.2%)	150 (55.4%)	.11
Multiparous	141 (51.8%)	121 (44.6%)	
Gestational age (wks)	38.1 ± 2.4 (24 – 41)	38 ± 2.5 (24 – 41)	.92
< 37 wks	32 (11.8%)	46 (17.0%)	.11
Diabetes mellitus	26 (9.6%)	35 (12.9%)	.28
PGDM	9 (3.3%)	8 (2.9%)	
GDM	17 (6.3%)	27 (10.0%)	
Hypertension	24 (8.8%)	34 (12.5%)	.08
Pre-pregnancy HTN	11 (4.0%)	8 (2.9%)	
PIH	13 (4.8%)	26 (9.6%)	
Smoking during pregnancy	20 (7.3%)	20 (7.4%)	>.999
Mode of CS			
Elective	214 (78.7%)	211 (77.9%)	.90
Emergency	58 (21.3%)	60 (22.1%)	
Previous CS	96 (35.3%)	87 (32.1%)	.49
Multiple pregnancy	5 (1.8%)	7 (2.6%)	.76
Duration of surgery (min.)	36.3 ± 9.0 (17 – 82)	36.7 ± 11.4 (17 –125)	.94
≤25	35 (12.9%)	34 (12.5%)	.86
25–50	218 (80.1%)	221 (81.5%)	
>50	19 (7.0%)	16 (6.0%)	
Surgeon experience			
Resident	106 (39.0%)	113 (41.7%)	.56
Assistant specialist	73 (26.8%)	77 (28.4%)	
Consultant	93 (34.2%)	81 (29.9%)	
Type of anesthesia			
Spinal	225 (82.7%)	221 (81.6%)	.81
General	47 (17.3%)	50 (18.4%)	
MSAF	20 (7.3%)	21 (7.7%)	.99
Pre-operative Hgb (g/dL)	12.2 ± 1.0 (8.3 – 14.9)	12.3 ± 1.1 (8.7 – 16.1)	.77
Post-operative Hgb (g/dL)	10.9 ± 1.0 (7.1 – 14.2)	11 ± 1.2 (6.5 – 14.6)	.39
Δ Hgb (g/dL)	1.3 ± 0.7 (0.1 – 3.5)	1.3 ± 0.9 (0.1 – 6.5)	.17
Blood transfusion	6 (2.2%)	4 (1.5%)	.75
Length of post-operative hospital stay (d)	4.3 ± 1.9 (3 – 14)	4.6 ± 2.1 (3 – 15)	.22

Data are expressed as mean ± SD/ (range) or as frequency (%).
BMI = body mass index; PGDM = pre-gestational diabetes mellitus; GDM = gestational diabetes mellitus; HTN = hypertension; PIH = pregnancy induced hypertension; CS = cesarean section; MSAF = meconium stained amniotic fluid; Hgb = hemoglobin concentration; Δ Hgb = change in hemoglobin concentration.

In order to identify the factors responsible for post-operative SSI in women after CS, univariate logistic regression, followed by multivariable logistic regression with backward selection based on the Akaike Information Criterion, were performed.

On the basis of the pilot study results, power analysis indicated that a sample size of 248 for each of the two groups was required to detect a difference in SSI proportion, with a power of 90% and $\alpha = 0.05$.

Results

During the study period, between June 2014 and April 2015, there were 1144 deliveries, including 605 cesarean

Table 2. Primary and Secondary Study Outcomes

	Study group (n = 272)	*Control group* (n = 271)	*p*
No. of patients with SSI (%)	5 (1.8)	14 (5.2)	.04
No. of patients with SSI and wound dehiscence (%)	1 (0.4)	2 (0.7)	>.99
No. of patients with SSI who required systemic antibiotic treatment (%)	0	4 (1.5)	.13
No. of patients with SSI who required hospital readmission (%)	0	3 (1.1)	.24
No. of patients with SSI who required surgical intervention (%)	0	0	-
	Study group (n = 5)	*Control group* (n = 14)	
Time of SSI occurrence (d)	7.4 ± 1.14 (6-9)	9.1 ± 3.6 (3–14)	.26
No. of ambulatory visits	4.6 ± 1.67 (2-6)	2.9 ± 1.1 (1– 4)	.02
Length of additional hospitalization (d)	0	8.2 ± 3.2 (5–11)	.22

Data are expressed as mean ± SD/ (range) or as frequency (%)
SSI = surgical site infection.

sections (52.9%), at the Department of Obstetrics, Gynecology and Oncology (Fig. 1). Among the women undergoing CS, 19 failed to meet the inclusion criteria: Two were <18 y of age, 11 were not in the capacity to or failed to consent to participation in the study, one patient had CS performed by a longitudinal skin incision, and five patients did not receive antibiotic prophylaxis. Out of the 586 patients who were deemed eligible for the study and who were randomly assigned into either the DACC group (study group, n = 296) or the SSD group (control group, n = 290), 43 (7.3%) failed to report for follow-up visits and were excluded from further analysis. In the final stage, the study and control groups consisted of 272 and 271 patients, respectively.

Table 3. Microorganisms Isolated from Surgical Site Infections during the Study Period from June 2014 to April 2015

	Study group	*Control group*
Microorganisms	*No. (%)*	*No. (%)*
Enterobacteriaceae	1 (9.1)	9 (56.25)
Klebsiella pneumoniae	0	3
Proteus mirabilis	0	1
Enterobacter cloacae	0	2
Escherichia coli	1	3
Coagulase-positive Staphylococci	2 (18.2)	1 (6.25)
MSSA	2	1
Coagulase-negative Staphylococci	1 (9.1)	1 (6.25)
MSSE	1	0
Staphylococcus hominis	0	1
Anaerobes	2 (18.2)	1 (6.25)
Bacteroides fragilis	1	0
Prevotella bivia	0	1
Peptoniphilus asaccharolyticus	1	0
Enterococcaceae	2 (18.2)	1 (6.25)
Enterococcus faecalis	2	1
Streptococcus sp.	2 (18.2)	0 (0)
Other	1 (9.1)	3 (18.75)
Total	11 (100)	16 (100)

MSSA = methicillin susceptible *Staphylococcus aureus*; MSSE, methicillin susceptible *Staphylococcus epidermidis*

Patient characteristics are presented in Table 1. There were no substantial differences between the DACC and the SSD groups with regard to patient demographics and perioperative course. Surgical site infections were observed substantially more often in the SSD group (Table 2). Incisional SSIs occurred during the first 14 post-operative days in 5.2% of patients from the control group as compared with 1.8% of women from the study group (p = 0.04). No statistically significant differences were found as far as the presence of post-operative wound dehiscence, receipt of systemic antibiotic therapy, or re-admission rates were concerned. Regardless of the fact that women who received the DACC dressing did not require systemic antibiotic therapy and additional hospitalization, the number of ambulatory visits was substantially higher in the study group as compared with the control groups, 4.6 vs. 2.9, respectively (p = 0.02) (Table 2). Mean time of additional hospitalization in the SSD group was 8.2 d. In both groups there were no cases of SSIs in patients with diabetes mellitus, both pre-existing before pregnancy and gestational, and with chronic arterial hypertension. All study participants were HIV-negative.

Enterobacteriaceae, coagulase-positive and negative *staphylococci*, anaerobes, *Enterococcaceae*, and *Streptococcus* sp. were the pathogens responsible for most SSI cases in both groups (Table 3). Microbiological analysis revealed strains of *Enterobacteriaceae* as the dominant group of pathogens isolated in patients from the SSD group, accounting for more than half of the identified microorganisms (56.25%). A similar correspondence was not observed in the DACC group, where *Enterobacteriaceae* constituted 9.1% of the isolated strains, with no dominant group of pathogens.

The univariate analysis revealed pre-pregnancy BMI of $\geq 30\,kg/m^2$ (odds ratio [OR] = 4.5; [95% CI: 1.3–14.8]; p = 0.009), pregnancy induced hypertension (OR = 5.1; [95% CI: 1.4–16.2]; p = 0.008), and smoking in pregnancy (OR = 5.0; [95% CI: 1.3–15.7]; p = 0.009) to be the factors that substantially increase the risk for SSI, and

Table 4. Univariate Analysis of Risk Factors for Surgical Site Infection in Females after Cesarean Section

	No. (%) of patients			
	SSI (n = *19*)	*No SSI* (n = *524*)	*OR (95% CI)*	*p*
Age (y)				
≤30	10 (52.6)	239 (45.6)	1.0	-
31–40	8 (42.1)	274 (52.3)	0.7 (0.23– 2.0)	.48
>40	1 (5.3)	11 (2.1)	2.2 (0.4 –17.9)	.41
Race				
Caucasian	18 (94.7)	519 (99.0)	1.0	-
Non-Caucasian	1 (5.3)	5 (1.0)	5.7 (0.1 –55.2)	.19
Weight gain during pregnancy (kg)				
≤10	7 (37.0)	132 (25.0)	1.0	-
>10	12 (63.0)	392 (75.0)	0.6 (0.2 – 1.8)	.28
Pre-pregnancy BMI (kg/m^2)				
BMI <25	9 (47.4)	360 (68.7)	1.0	-
BMI ≥25 and <30	4 (21.0)	111 (21.2)	0.99 (0.23– 3.2)	>.999
BMI ≥30	6 (31.6)	53 (10.1)	4.5 (1.3 –14.8)	.009
Parity				
Primiparous	14 (73.7)	267 (51.0)	2.7 (0.9 – 9.7)	.06
Gestational age				
< 37 wks	5 (26.3)	73 (13.9)	2.2 (0.6 – 6.7)	.17
Hypertension				
PIH	5 (26.3)	34 (6.5)	5.1 (1.4 –16.2)	.008
Smoking during pregnancy	5 (26.3)	35 (6.7)	5.0 (1.3 –15.7)	.009
Mode of CS				
Elective	13 (68.4)	412 (78.6)	1.0	-
Emergency	6 (31.6)	112 (21.4)	1.7 (0.5 – 4.9)	.27
Previous CS	3 (15.6)	180 (34.4)	0.4 (0.7 – 1.28)	.14
Multiple pregnancy	2 (10.5)	10 (1.9)	6.0 (0.6 –31.6)	.06
Duration of surgery (min.)				
≤25	4 (21.0)	65 (12.4)	1.0	-
>25	15 (79.0)	459 (87.6)	0.53 (0.16– 2.27)	.28
Surgeon experience				
Resident	8 (42.1)	211 (40.3)	1.0	-
Assistant specialist	5 (26.3)	145 (27.7)	0.9 (0.2 – 3.2)	>.999
Consultant	6 (31.6)	168 (32.0)	0.9 (0.3 – 3.2)	>.999
Type of anesthesia				
Spinal	14 (73.7)	432 (82.4)	1.0	-
General	5 (26.3)	92 (17.6)	1.7 (0.5 – 5.1)	.36
MSAF	3 (15.8)	38 (7.2)	2.4 (0.4 – 8.9)	.17
Pre-operative Hgb				
≤12 g/dL	6 (31.6)	191 (36.4)	0.8 (0.2 – 2.3)	.81
Post-operative Hgb				
≤10 g/dL	3 (15.8)	97 (18.5)	0.8 (0.15– 3.0)	>.999
Δ Hgb				
≥3g/dL	1 (5.3)	9 (1.7)	3.2 (0.07–25.1)	.30
Length of post-operative hospital stay (d)				
≤5	13 (68.4)	393 (75.0)	1.0	-
6–10	5 (26.3)	123 (23.5)	1.2 (0.3 – 3.8)	.78
>10	1 (5.3)	8 (1.5)	3.7 (0.08–31.9)	.27
Dressing type				
SSD	14 (73.7)	257 (49.1)	1.0	-
DACC	5 (26.3)	267 (50.9)	0.3 (0.09– 1.03)	.04

SSI = surgical site infection; BMI = body mass index; PIH = pregnancy induced hypertension; CS = cesarean section; MSAF = meconium stained amniotic fluid; Hgb = hemoglobin concentration; Δ Hgb = change in hemoglobin concentration; SSD = standard surgical dressing; DACC = dialkylcarbamoyl chloride-impregnated dressing; CI = confidence interval; OR = odds ratio.

application of the DACC impregnated dressing as the factor that lowers the risk (OR =0.3; [95% CI: 0.09–1.03]; p = 0.04) (Table 4).

In order to identify independent risk factors for SSI, a separate multivariable logistic regression with backward selection was performed. The following parameters were found to influence the risk for SSI: Pre-pregnancy BMI (aOR = 1.08; [95% CI: 1.0–1.2]; $p < 0.05$), smoking in pregnancy (aOR = 5.34; [95% CI: 1.6–15.4]; $p < 0.01$) and SSD application (aOR = 2.94; [95% CI: 1.1–9.3]; $p < 0.05$).

Total estimated cost of SSI prophylaxis and treatment was greater in the control group as compared with the study

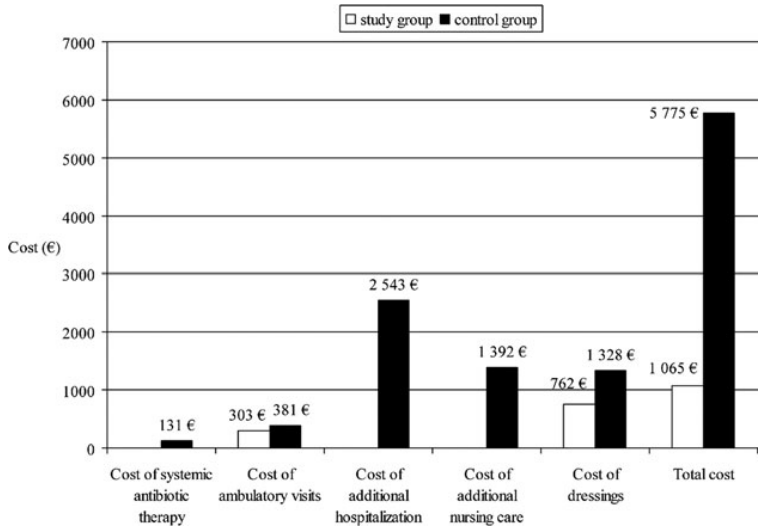

FIG. 2. Cost of treatment attributable to surgical site infection after cesarean section by dressing type.

group, and amounted to 5775 EUR vs. 1065 EUR, respectively (Fig. 2). In the study group it comprised only the cost of ambulatory visits, whereas in the control group total cost encompassed additional expenses because of prolonged hospitalization and additional nursing care. Similarly, systemic antibiotic treatment with metronidazole, cefuroxime, ceftriaxone, amoxicillin, ciprofloxacin, or gentamicin used alone or in combination was necessary only in patients in the control group.

Discussion

The presented study was a single-center, randomized controlled trial, aiming to evaluate the efficacy of DACC impregnated dressings to prevent SSI in women after CS. To the best of our knowledge, it has been the first prospective study on the use of DACC dressings in a large cohort of pregnant women.

Our results confirmed effectiveness of the DACC dressings in SSI prevention after CS. Application of the hydrophobic dressing resulted in a decreased rate of SSI and its considerably milder course, with no need for systemic antibiotic therapy and hospital readmissions. As a consequence, the total cost of SSI treatment was lower in the DACC group and was a result of ambulatory visits only. Despite the fact that the total number of the ambulatory visits was substantially higher in the study group, the dominant element in the total treatment cost was the length of additional hospitalization, with mean duration of 8 d in the group with SSD.

Multivariable logistic regression analysis revealed obesity, smoking, and the use of a standard occlusive dressing as the three independent factors that increase the risk for incisional SSI after CS. The adverse effects of the first two factors have been well-documented in the literature [2,3,5,7,8]. In case of obesity, excessive thickness of subcutaneous tissue is believed to cause tissue hypoperfusion and hypoxygenation, impeding the healing process and antibiotic penetration [24]. The risk of SSI is often additionally increased by the presence of hyperglycemia, prolonged surgery time because of technical difficulties, the need for a longer skin incision, and more blood loss. Also, proper wound hygiene and care may be hampered by the location of the incision between skin folds, what may predispose to the development of infection. As far as smoking is concerned, the components of tobacco smoke cause tissue hypoxia, impair the function of inflammatory cells, and limit fibroblast proliferation and migration, thus delaying wound healing [25–27].

The type of dressing used in prevention of SSI after obstetric operations is of the utmost importance from the point of view of the study goals. Similarly to subcutaneous drains or surgical staples used for skin closure, the type of the applied dressing may affect the risk of SSI [2,5]. Obtained results revealed an almost three-fold increase of SSI risk in patients who received the SSD.

Microorganisms responsible for SSI were similar in both groups, with the exception of more numerous *Enterobacteriacae* strains found among the control groups, which may be explained by the fact that approximately 25% of *Enterobacter* spp. strains isolated from surgical incisions are characterized by high CSH, whereas hydrophobic properties are found in 88% of the *Enterobacter cloacae* strains alone [28]. In case of *Klebsiella pneumoniae*, CSH is affected by the presence of O-antigen lipopolysaccharide or polysaccharide capsule, making bacteria more hydrophilic and, as a result, less susceptible to adhesion to the hydrophobic surface of the dressing [29]. Neither the abovementioned properties of bacterial strains nor the effect of the remaining factors on the CSH of the isolated pathogens were the subject of the investigation. It has been proven that the use of octenidine solution, just as bacterial culture in carbon dioxide atmosphere in the presence of serum, resembling wound conditions under an occlusive dressing, increase CSH, contrary to antibiotics used in pre-operative prophylaxis [11,16,30].

Our study is subject to several limitations, including the fact that the effectiveness of the impregnated dressings was analyzed in a group of women undergoing CS, which, unlike most surgical patients, constitute young population with few comorbidities. Also, the observed SSI incidence after CS

most probably does not reflect the total SSI rate because of the fact that analysis included only superficial and deep SSI, as well as shorter than recommended by the CDC period of observation. Exclusion of organ/space SSI from the analysis was imposed by the fact that the effect of the dressing on the incidence of such infections after CS is limited and the shortened time of the observation, from the recommended 30 d to 14 d, was conditioned by lack of the possibility of effective medical supervision and low patient compliance after that time, as described by Wilson et al. [4]. At the same time, the literature reports indicate that superficial and deep SSIs account for 93%–100% of all cases of SSI following CS, with 78%–100% occurring within 14 d of the surgery [2–4,6,7]. As the subject of the study included only superficial and deep SSI such risk factors as number of vaginal examinations, duration of labor or pre-term rupture of membranes were not included in the analysis, taking into account their correlation with organ/space infections.

To conclude, the use of a DACC-coated dressing decreased the SSI rates among patients after CS and proved its cost-efficacy. Weight reduction before conception, abstaining from smoking in pregnancy, and application of dressings that are effective in SSI prophylaxis, are the key factors which might prevent SSIs after CS.

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Author Disclosure Statement

All authors report no conflicts of interest relevant to this article.

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infection occurs in approximately 1.8–9.2% of patients after a CS, being one of the most common complications that may lead to wound dehiscence or systemic infections in case of lack of sufficient prophylaxis or inappropriate treatment [2–8]. Increased morbidity, prolonged hospitalization time, increased rate of hospital readmissions and growing treatment costs are all consequences of the above [9].

Dressings impregnated with dialkylcarbamoyl chloride (DACC) are an innovative approach used in the treatment of venous, arterial, diabetic and pressure ulcers, burns, post-traumatic and post-operative wounds [10–13]. Dialkylcarbamoyl chloride, a hydrophobic derivative of fatty acids, irreversibly binds microorganisms as a result of an interaction between hydrophobic particles in the presence of the aqueous medium, therefore allowing for elimination of bacteria and fungi during dressing replacement. The mechanism of action is based on the fact that the majority of pathogens isolated from infected wounds express high to moderate cell surface hydrophobicity (CSH), which on the one hand enables cell attachment and infection initiation by microbes, but on the other hand facilitates their aggregation on the surface of a hydrophobic dressing under moist wound conditions [14–17]. As a result, the number of pathogenic microorganisms in the wound bed is significantly reduced, and their proliferation as well as toxin production is limited [18, 19]. Additionally, the results of recently published *in vitro* studies demonstrated a separate mechanism of action present within hydrophobic dressings, responsible for accelerated wound healing, namely stimulation of fibroblast proliferation and migration [20]. Due to the fact that dressings have a solely physical mechanism of action that is not accompanied by a release of additional antimicrobial substances, the risk of cytotoxicity and sensitization has been eliminated and there are no risks associated with resistance development among bacteria and fungi responsible for wound infections. As a result, hydrophobic dressings can be used safely and without time restrictions, including in women during the puerperal and lactation period.

Taking into account the continuously increasing number of CS and a wide spread of factors responsible for wound healing disturbances in the population of women of reproductive age, such as obesity, diabetes and nicotinism, it is necessary to search for new, more effective methods to prevent infections of surgical wounds.

This study aimed to assess the efficacy of dressings impregnated with DACC in the prevention of incisional surgical site infections in patients undergoing cesarean section.

Material and methods

A single-blinded randomized, controlled pilot study was conducted at the Department of Obstetrics, Gynecology and Oncology, Mazovian Bródno Hospital, Warsaw, Poland between December 2013 and March 2014. Mazovian Bródno Hospital is a tertiary care and academic hospital for the Medical University of Warsaw, performing approximately 1300 deliveries per year, with the CS rate of 51.8% in the study period. Expedited approval for this study was obtained from the Ethics Committee at the Medical University of Warsaw, and written informed consent was gained from all participants. Patients after a planned or emergency CS were enrolled in the study. The inclusion criteria were as follows: age above 18 years, single or multiple pregnancy, mental and physical capability to provide written consent for participation in a clinical trial, and patient's declared compliance with the study plan. Women less than 18 years old or unable to give informed consent were excluded from the study. Patients were randomized into 2 groups depending on the dressing that had been applied. Patients in whom after a cesarean section a dressing impregnated with DACC (Sorbact Surgical Dressing, ABIGO Medical AB, Sweden) was used constituted the study group, whereas patients who received a standard surgical dressing were included in the control group. Simple randomization with the 1 : 1 allocation ratio performed by an operating theater nurse was used to alternate patients enrolled for alternate dressings – even number: DACC-impregnated dressing; odd number: standard surgical dressing.

Data on patient characteristics, pre-, peri- and postoperative course were taken from hospital medical records. The analysis included age, race, parity, pre-pregnancy weight, weight gain during pregnancy, pre-pregnancy body mass index (BMI), gestational age, history of pre-gestational or gestational diabetes mellitus, chronic or pregnancy-induced hypertension, previous CS, tobacco use during pregnancy, mode of CS (planned/emergency), duration of surgery, surgeon experience, hemoglobin levels prior to and 24 h after surgery, and hospitalization time after surgery. An emergency CS was defined based on the time between a decision and skin incision below 30 min. The surgery time was measured between skin incision and skin closure. The hospitalization time after surgery was the number of days from the CS (day 0) to the patient's discharge from hospital. The surgeon's experience was determined based on the medical position and work experience, and classification to one of three groups was performed: resident – a medical doctor during specialization in obstetrics, an obstetrics specialist working for 5 years at most, or an obstetrics specialist working for more than 5 years.

In all patients enrolled in the study a transverse skin incision (Pfannenstiel) followed by a transverse uterine incision in its lower segment was applied. For fascial, subcutaneous tissue and skin incision closure, continuous antibacterial braided absorbable suture (Vicryl Plus 1, Ethicon, USA), single monofilament absorbable suture (Monosyn 2/0, B. Braun Melsungen AG, Germany) and subcuticular continuous monofilament non-absorbable suture (Prolene 2-0, Ethicon, USA), respectively, were used. All participants received an intravenous antibiotic dose as prophylaxis – 1 g of cefazolin 0–30 min prior to the start of surgery. Additionally, in all patients wound irrigation with an octenidine solution (Octenisept, Schülke & Mayr GmbH, Germany) was performed prior to the closure of subcutaneous tissue. The surgical team was blinded to the dressing type until skin closure.

Pursuant to the valid study protocol, in all subjects dressings remained in situ for the first 48 h after surgery unless there were reasons for dressing replacement such as excessive wound bleeding and/or dressing detachment. After 48 h dressings were removed in both groups, and the first clinical wound evaluation was performed. According to the management strategy at the clinic, patients were discharged on the third day after surgery and were recommended to re-visit on day 7 in order to have skin suture removed. The second clinical wound assessment was performed at this visit. The third and final wound evaluation was scheduled on day 14 after a CS. On the discharge day all patients for whom less than 14 days had passed since surgery received detailed instructions regarding surgical site infections (SSIs) and were informed about the need to report at hospital in case at least one of the following symptoms was observed: fever, suppurative secretion from the surgical site, redness, edema, warmth, pain or tenderness of the surgical site area. Patients who did not report for follow-up visits 7 and 14 days after a CS were excluded from the final analysis.

At each surgical wound evaluation scheduled in the study, symptoms of superficial or deep SSI were analyzed according to the CDC criteria [2]. Additionally, the presence of surgical wound dehiscence, defined as separation of the skin, subcutaneous tissue and/or fascia resulting from an incisional SSI, was evaluated. Other parameters subject to the analysis in the group of patients with wound infection were as follows: time of wound infection occurrence (defined as the period from day 0 to the day when first infection symptoms developed), need for systemic antibiotic treatment, need for hospital readmission and need for a surgical intervention. All surgical wound evaluations during patient hospital stay, follow-up visits and self-referral to hospital, as well as SSI classification according to the CDC criteria, were performed by one of the authors (PS).

From all patients with clinical symptoms of SSI, wound swabs were collected in order to perform a microbiological analysis and to identify the responsible pathogen (Copan Sterile Transport Swab, Copan Diagnostics, USA).

CONSORT 2010 guidelines for randomized controlled trials including a checklist and flow diagram were applied to ensure the quality of the conducted study [21].

Statistical analysis

The primary outcome in this study was development of superficial or deep SSI within the first 14 days after a CS. In order to assess whether individual pre-, peri- and post-operative variables affect the development of surgical site infection in women undergoing CS, a logistic regression model with forward selection was designed. The model included the following variables: age, race, parity, gestational age, pre-pregnancy weight, weight gain during pregnancy, pre-pregnancy BMI, pre-gestational or gestational diabetes mellitus, chronic or pregnancy-induced hypertension, previous CS, tobacco use during pregnancy, mode of CS, duration of surgery, surgeon experience, hemoglobin levels prior to and 24 h after surgery, hospitalization time after surgery as well as dressing type.

A statistical analysis was performed using SPSS 17.0 for Windows software (SPSS Inc, Chicago, IL). The Shapiro-Wilk test was used for a normality analysis. Continuous variables were compared by the *t* test, or the Mann-Whitney *U* test, as appropriate. For categorical variables the χ^2 test or the Fisher exact test were applied. Statistical significance was set at $p < 0.05$.

Results

In the period between December 2013 and March 2014 at the Department of Obstetrics, Gynecology and Oncology 193 patients underwent CS, and 31 of them did not meet the study inclusion criteria. One hundred and sixty-two participants were randomized, however 20 women (10 in each group) did not report for scheduled follow-up visits and were excluded from the analysis, leaving a total of 142 eligible patients. The number of participants evaluable for final analysis was equal in both groups – 71 patients in the group with a DACC-impregnated dressing (study group) and in the group with a standard surgical dressing (control group). The patient recruitment process and randomization are summarized in the CONSORT 2010 flow diagram (Figure 1).

Eighteen (25.3%) patients in the study group and 17 (23.9%) patients in the control required

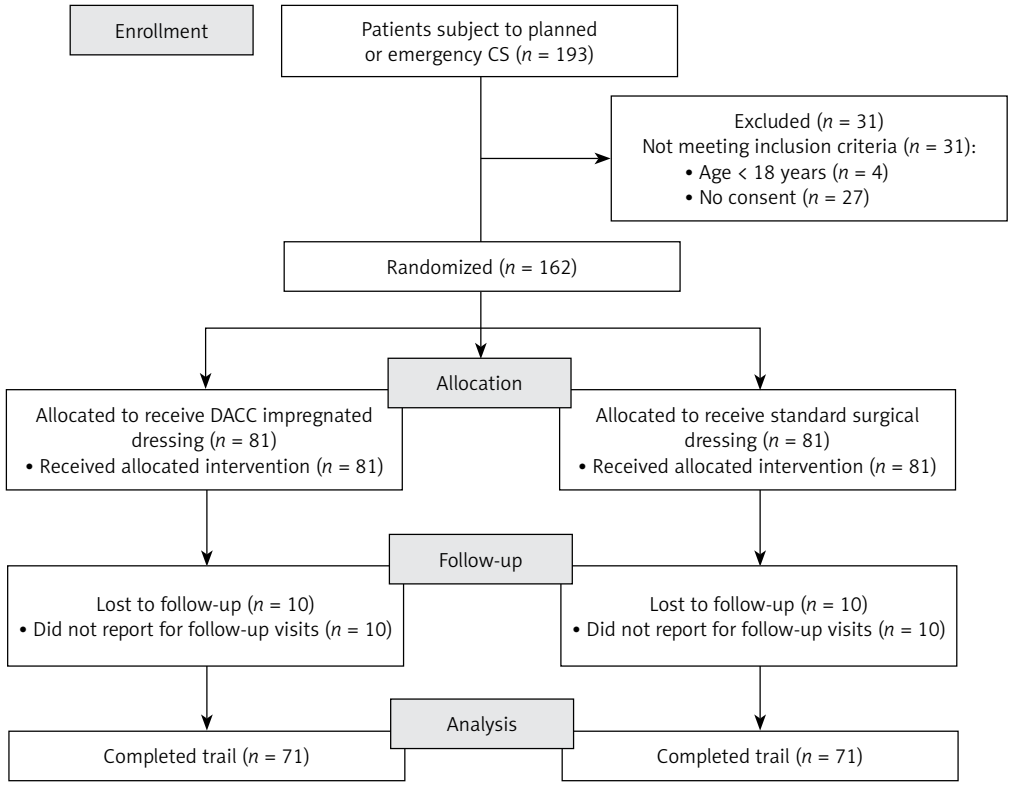

Figure 1. CONSORT 2010 flow diagram of the recruitment process and randomization

CS – cesarean section, DACC – dialkylcarbamoyl chloride.

dressing replacement within the first 48 h following surgery as a result of wound hemorrhage (p = 0.84). There were no cases of dressing detachment in both groups.

Demographic, peri- and postoperative characteristics are shown in Table I. There were no significant differences between the two groups.

Primary and secondary study outcomes are summarized in Table II. The rate of surgical site infections in the group with a DACC-impregnated dressing was 2.8% (2 cases of superficial SSI), whereas in the group with a standard surgical dressing it was 9.8% (6 cases of superficial and 1 case of deep SSI) (p = 0.08). One (1.4%) patient in the control group developed surgical wound dehiscence due to infection. The same patient required rehospitalization and a surgical intervention due to necrotizing fasciitis. In the study group there were no cases of wound dehiscence, and none of the patients who received a DACC-impregnated dressing required hospital readmission and/or surgical intervention. In 5 (7.0%) cases of wound infection in the control group systemic antibiotic treatment was instituted, whereas it was not necessary in the study group (p = 0.03). The mean time to first symptoms of wound infection was 10.5 and 8.8 days in the study and control group, respectively (p = 0.24).

The microbiological analysis of cultures from infected wounds demonstrated *Staphylococcus epidermidis* in 2 and 3 cases of SSIs in the study and control group, respectively. In the remaining patients in the control group wound infection was caused by *Pseudomonas aeruginosa* (2×), *Streptococcus* sp. (1×) and methicillin-resistant *S. epidermidis* (1×).

The logistic regression model used to determine the effects of selected parameters on SSI development was statistically significant ($\chi^2(1) = 5.52$; p = 0.019) and explained 10.1% of observed variance for the dependent variable (R^2 Nagelkerke = 0.101). The Hosmer-Lemeshow test demonstrated that the model is appropriate for data collected: $\chi^2(8) = 6.13$; p = 0.632. According to the logistic regression analysis, only the pre-pregnancy BMI was a significant predictor of wound infection (B = 0.13; W = 5.96; p = 0.015; exp(B) = 1.139; 95% CI: 1.026–1.265).

Discussion

This study aimed to assess the efficacy of dressings impregnated with DACC in the prevention of wound infection in patients after a CS. To our knowledge there have not been any studies published to date on the use of such dressings in the prevention of surgical wound infection. The re-

Table I. Demographic, peri- and postoperative characteristics

Parameter	Study group (n = 71)	Control group (n = 71)	P-value
Age [years]	30.9 ±4.5 (19–41)	31.2 ±5.1 (19–43)	0.64
Race:			> 0.999
Caucasian	70 (98.6)	71 (100)	
Non-Caucasian	1 (1.4)	0 (0)	
Pre-pregnancy weight [kg]	67.3 ±12.4 (48–116)	68.8 ±16.9 (48–116)	0.78
Weight gained during pregnancy [kg]	14.4 ±5.6 (0–27)	13.3 ±5.6 (3–30)	0.26
Pre-pregnancy BMI [kg/m²]:	24.3 ±4.1	25.3 ± 6.0	0.77
< 25	44 (62.0)	41 (57.8)	0.61
≥ 25 and < 30	18 (25.3)	17 (23.9)	0.84
≥ 30 and < 40	9 (12.7)	10 (14.1)	> 0.999
≥ 40	0 (0)	3 (4.2)	0.24
Parity:			
Nulliparous	24 (33.8)	34 (47.9)	0.09
Gestational age [weeks]	37.9 ±2.7 (24–41)	38.2 ±2.2 (28–41)	0.45
Diabetes mellitus:	7 (9.8)	7 (9.8)	> 0.999
PGDM	2 (2.8)	4 (5.6)	0.68
GDM	5 (7.0)	3 (4.2)	0.72
Hypertension:	7 (9.8)	7 (9.8)	> 0.999
Pre-pregnancy HTN	1 (1.4)	3 (4.2)	0.62
PIH	6 (8.4)	4 (5.6)	0.74
Tobacco use during pregnancy	4 (5.6)	5 (7.0)	> 0.999
Mode of CS:			
Planned	53 (74.7)	51 (71.8)	0.70
Emergency	18 (25.3)	20 (28.2)	0.70
Previous CS	19 (26.8)	17 (23.9)	0.70
Duration of surgery [min]	37.2 ±8.0 (21–57)	35.3 ±12.7 (17–105)	0.06
Surgeon experience:			
Resident	32 (45.1)	29 (40.9)	0.61
Specialist ≤ 5 years	16 (22.5)	16 (22.5)	> 0.999
Specialist > 5 years	23 (32.4)	26 (36.6)	0.60
Pre-operative hemoglobin [g/dl]	12.1 ±0.9 (9.8–14.1)	12.0 ±1.0 (9.4–14.0)	0.68
Post-operative hemoglobin [g/dl]	10.7 ±1.2 (7.6–13.5)	10.7 ±1.1 (8.0–12.7)	0.64
Median (range) time of post-operative hospital stay [days]	4.4 ±2.3 (3–15)	4.5 ±2.5 (3–17)	0.59

Data are expressed as mean ± SD/(range) or as frequency (%). BMI – body mass index, PGDM – pre-gestational diabetes mellitus, GDM – gestational diabetes mellitus, HTN – hypertension, PIH – pregnancy-induced hypertension, CS – cesarean section.

sults of the pilot study indicated a decreasing tendency of the observed surgical site infection rate in patients who received DACC dressings. However, when the results obtained were compared to a standard surgical dressing, statistical significance was not achieved, and in order to draw final conclusions it is necessary to perform studies in a larger group of patients. From the point of view of health-care system economics and cost reduction, in the study group there were no

Table II. Primary and secondary outcomes

Parameter	Study group (n = 71)	Control group (n = 71)	P-value
No. of patients with SSI (%)	2 (2.8)	7 (9.8)	0.08
No. of patients with SSI and wound dehiscence (%)	0 (0)	1 (1.4)	0.50
No. of patients with SSI who required systemic antibiotic treatment (%)	0 (0)	5 (7.0)	0.03
No. of patients with SSI who required hospital readmission (%)	0 (0)	1 (1.4)	0.50
No. of patients with SSI who required surgical intervention (%)	0 (0)	1 (1.4)	0.50
Median (range) time of SSI occurrence [days]	Study group (n = 2)	Control group (n = 7)	
	10.5 (10–11)	8.8 (6–13)	0.24

Data are expressed as frequency (%). SSI – surgical site infection.

cases of surgical wound dehiscence and none of the patients required rehospitalization or surgical intervention. Additionally, patients in whom a hydrophobic dressing was applied required systemic antibiotic therapy significantly less frequently. As a result, the use of hydrophobic dressings in standard management strategies for wounds in patients undergoing a CS may contribute to reduced total costs of treatment.

The observed incidence of wound infection after a CS, namely 2.8% or 9.8% depending on the type of dressing used, is similar to results observed by other authors [3–8]. The obtained results probably do not reflect the total SSIs rate due to the fact that the analysis was limited to superficial and deep infections without the organ/space group, and there was a 14-day follow-up after surgery, contrary to the recommended 30-day period presented in the CDC criteria [2]. Introduced changes were a result of the assumption that the rate of organ/space SSI after a CS is low, and dressings have an insignificant effect on their occurrence. The fact that within the scheduled 2 weeks of a follow-up wound infection diagnosis was performed only by a trained healthcare provider also was of importance. Our assumptions are supported by literature data reporting that superficial and deep wound infections after a CS constitute 93–100% of all SSIs, and 77–95% of them develop within the first 14 days after the surgery [4–7]. In order to provide additional verification of the results, a hospital medical database was analyzed to search for patients referred to an outpatient clinic with symptoms suggesting SSIs, and in whom the period since the surgery ranged between 15 and 30 days. There were no records corresponding to such criteria. At the same time, the study by Whitby *et al.* demonstrated a high negative predictive value of patient wound self-monitoring exceeding 97%, in case of lack of infection symptoms and irrespective of the patient knowledge regarding SSIs [22]. There is a slight likelihood of an error of verification performed, however, as patients might have reported to another medical centre.

According to the analysis of risk factors for surgical wound infections, only pre-pregnancy BMI was a statistically significant variable. The fact that obesity increases the risk of wound infection after a CS has been confirmed by many publications [5–8]. It is presumed that excessive thickness of the subcutaneous tissue favors hypoperfusion of tissues, resulting in their ischemia and making antibiotic therapeutic concentration difficult to achieve [23]. An additional aspect is the fact that obesity is often accompanied by carbohydrate metabolism disturbances and prolonged surgery time due to technical difficulties and the need to perform a longer skin incision [23]. It seems that due to a constantly increasing rate of obese or overweight women subject to a CS it is justified to verify and adjust prophylactic doses of antibiotics administered prior to surgery in this group of patients. Supervision by a dietician may also be of importance in the period prior to and during pregnancy.

Lack of confirmed statistical significance for other remaining risk factors for SSIs, such as diabetes, prolonged surgery time, surgeon experience or emergency mode of CS in the present study is probably a result of a too small study group compared to previous publications [5–8].

The microbiological analysis of wound cultures indicated that the main pathogen responsible for infection in both groups is coagulase-negative *Staphylococcus epidermidis*, strains of which exhibit high variability with regard to CSH, and hydrophilicity is more predominant [17, 24–26]. In the group with hydrophobic dressings and in the group with a standard surgical dressing there were no cases of infection caused by *S. aureus*, whereas in the latter group the presence of *Pseudomonas aeruginosa* was confirmed twice. This last phenomenon can be explained by an observed increase in CSH of *P. aeruginosa* in carbon dioxide atmosphere and in the presence of serum [17]. These conditions, similar to the wound en-

vironment under an occlusive dressing, may contribute to increased absorption of bacteria due to hydrophobic interactions.

In conclusion, it is commonly known that infection impairs and delays wound healing due to damage of healthy cells by toxins released by pathogenic microorganisms and enzymes from inflammatory cells. Only in the case of spreading or systemic infection is it recommended to use antibiotics in combination with topical antimicrobial treatment. However, when only wound contamination or colonization occurs and the healing process progresses, the use of methods as above is not recommended due to systemic action and a possibility of resistance development. Surgical wounds in obstetrics are classified as clean-contaminated wounds; therefore in infection prophylaxis it is recommended to use local methods and preferably those that limit the release of additional antimicrobial agents due to lactation. This study has demonstrated that DACC-impregnated dressings can be applied for the prevention of SSIs in women after a CS based solely on a physical mechanism of action. Taking into account the constantly increasing rate of patients subject to CS, and the fact that a considerable number of women of reproductive age have risk factors for wound infections, further attempts to use such dressings are justified and the obtained study results are promising. The study presented above was preliminary; a randomized, controlled trial with a larger group of patients is ongoing, and its aim is to draw final conclusions.

Conflict of interest

The authors declare no conflict of interest.

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Silver-containing dressings are used worldwide for the local management of colonised or infected leg ulcers. We routinely use a silver-containing Hydrofiber dressing. (SCH: Aquacel Ag, ConvaTec, NJ, US). The dressing releases silver ions on the wound bed or inside the dressing, these need to come into contact with and get inside bacteria to exert their bactericidal action. Bacterial destruction may result in the release of substances capable of prolonging the inflammatory response. Silver ion release has to be slow in order to provide a long lasting antimicrobial effect.

Systemic uptake of silver ions with deposition in organs like liver and kidney has been demonstrated.[9] Even if silver's systemic toxicity seems very low, there is no clear evidence about the effects of long-term exposure to high levels.[9] Another concern when using silver dressings is that silver at higher concentrations may exert a local cytotoxic effect binding fibroblasts and keratinocytes resulting in delayed healing.[10] Finally, the most important concern, is the onset of bacterial resistance to silver, which has been reported for *Escherichia coli*, *Klebsiella pneumoniae*, *Enterobacter cloacae*, *Pseudomona aeruginosa*, *Proteus mirabilis* and *Citrobacter freundii*.[11] Silver resistance determinants are often located on mobile genetic elements, facilitating their spread.[12] Even if the risk of widespread resistance to silver in wound care seems low, it has to be carefully monitored.[13]

As concerns persist about silver's potential toxicity, and the risk of bacterial resistance to silver,[9] we wanted to explore the clinical efficacy of a microorganism-binding (MB) dressing (Cutimed Sorbact, BSN Medical; Hamburg Germany), available locally for the treatment of critically colonised or infected wounds. MB dressings have antimicrobial capabilities. The dressing, which is designed to be in contact with the wound bed, is coated with dialkylcarbamoyl chloride (DACC) making the dressing hydrophobic. Wound bacteria are largely hydrophobic in nature and when in proximity to the hydrophobic dressing become bound to the dressing and are removed from the wound bed with dressing change. The result is a reduced wound bacterial load.[14] The antimicrobial properties of MB dressings are based on a physical effect; as a result, no bacterial resistance is expected or has been demonstrated.[15]

Objective

The aim of our study was to evaluate the efficacy of MB versus SCH dressings, before surgical management with skin grafting, in controlling the bacterial load of heavily colonised or locally infected chronic leg ulcers.

Materials and methods

This was a comparative, randomised, single centre pilot study. Patients with vascular leg ulcers (venous and arterial) and considered suitable for wound management with skin grafting were recruited for the study.

Signed informed consent was obtained from patients. The study complied with the Helsinki Declaration and the rules of the local ethical committee.

Inclusion criteria

Patients older than 18 years, of both genders, with critically colonised (multiplying bacteria causing delayed healing without sign of infection) or locally infected (multiplying bacteria with sign of local tissue damage) ulcers of vascular aetiology, duration ≥6 months and ankle brachial pressure index (ABPI)>0.6.

Exclusion criteria

Patients were excluded if they were younger than 18 years, had ulcers without signs of critical colonisation or infection, had ulcers of immunological or diabetic origin, were receiving cortisone or immunosuppressive treatment, had a ulcer duration <6 months, or had an ABPI<0.6.

Treatment protocol

Following inclusion, patients were randomly, using List Randomizer, assigned to treatment with SCH (20 patients) or MB dressings (20 patients). After an observation period of 4 days, during which time dressings were changed daily, patients were taken to the operating room for a planned skin grafting procedure. In cases of an incomplete wound bed preparation, with some areas of ulcer bed still covered by slough or necrotic tissue, sharp debridement was performed before skin grafting.

For the purpose of the present comparative study, the type of dressing was the only modification introduced to the management protocol. All products had the CE mark and were used according to the manufacturers' instructions.

Inelastic compression was used on all patients throughout the treatment period before and after the skin grafting. The level of compression was adapted individually depending on the ulcer aetiology and the peripheral vascular conditions. Patients with venous leg ulcers had compression up to 40mmHg,[16] while patients with arterial leg ulcers had lower levels of compression. In no case did the compression level exceed 40mmHg.[16]

The primary outcome was the ulcer bacterial load. Secondary outcomes were:

- Ease of dressing application and removal
- Treatment related pain variation
- Adverse events.

Primary outcome bacterial quantification

At inclusion (D0) and upon conclusion of the observation period (D4) swab samples from ulcer beds were taken in order to quantify bacterial load. After cleansing of the ulcer bed with Ringer's solution,

samples were taken from clinically chosen 1cm² areas by pressing and rotating the swab tip uniformly. In some cases, marks were made on the periwound skin in order to identify the same area for further swabbing procedures. Swabs were transferred to the laboratory and cultured for aerobic bacteria on Agar plates. The results were checked after 5 days. No antibiotics were administered to any patients before or during the evaluation period.

Secondary outcomes

Ulcer-related pain was evaluated using a visual analogue scale (VAS) where 0 represented absence of pain and 10 represented agonising pain.

Two nurses and one doctor provided their opinion about the features of the dressing, its conformability and ease of use.

Statistical analysis

Given the exploratory nature of the study we did not establish or test any hypothesis. Data were analysed using descriptive statistics and comparative tests including Student's t-tests to analyse differences between groups regarding demographic data, wound size, ulcer duration time, pain scores, bacterial loads at D0 and D4. ANOVA tests were used to analyse bioburden variation between D0 and D4 within and between groups, with p values <0.05 considered statistically significant.

Results

There were 20 patients allocated to each group with similar demographics in each, gender (16 male, 24 female) and age (69.5 ± 13.5 years). The aetiology of the lesions was also similar—in each group, 15 patients presented with venous leg ulcers and five with arterial leg ulcers (Tables I and II).

All patients completed the study. Surgical sharp debridement was not required in any case.

The statistical analysis found no significant difference between groups regarding wound size (p=0.48), ulcer duration time (p=0.47) or bacterial load at D0 (p=0.21; Tables III, IV and Fig 1).

Staphylococcus aureus, methicillin-resistant *Staphylococcus aureus* (MRSA), *Pseudomona aeruginosa*, *Enterococcus faecalis*, *Escherichia coli*, *Klebsiella*, *Enterobacter cloacae*, and *Proteus mirabilis* were most frequently found on the ulcer beds. In general we found a polymicrobial burden with bacterial species equally distributed in the two groups. The recorded data does not allow us to make any further comparison between bacteria species.

Primary outcome bacterial quantification

The average bacterial load was similar in both groups at D0, that is, 9.1 x 10^5CFU/cm² and 8.5 x 10^5CFU/cm² in the SCH and MB groups, respectively. After analysing bacterial load within each group, the results showed a significant reduction of bacterial burden at D4 in both groups. In the SCH group, the average bacterial load reduction was 41.6%, with a reduction of 73.1% in the MB group. When comparing bacterial load between groups at D4, the reduction was significantly higher in the MB group (p< 0.0001; Fig 1).

Secondary outcomes

Dressing application and removal was found to be atraumatic and simple for both dressing types. Average ulcer-related pain scores were 4.65 and 4.75 at D0 in the SCH and MB groups, respectively. Pain scores decreased in both groups, –35% in the SCH group and –38% in the MB group. The statistical analysis found no significant difference between groups at D0 (p=0.41) or at D4 (p=0.89; Fig 2).

Of the 40 patients, 20 (10 SCH and 10 MB) required analgesics before treatment. At D4, only 4 patients in the SCH group and 3 in the MB group still required analgesics.Only four patients in the SCH group and five in the MB group needed more than one piece of the dressing at each dressing change. Using more than one piece of the dressing did not have any effect on bacterial load reduction.

Two patients in the SCH group reported intense burning following the application of the dressing. The burning sensation lasted for a few hours, then disappeared without further problems and without the need for analgesics.

No serious adverse events related to the dressings were seen during the present study.

Discussion

Clinical practice has demonstrated that the majority of leg ulcers heal within 4–6 months when correctly

Table I. Ulcer aetiology and gender distribution

Group	Aetiology (n)	Male (n)	Female (n)	Total (n)
MB	Venous	5	10	15
	Arterial	4	1	5
SCH	Venous	5	10	15
	Arterial	2	3	5
TOTAL		**16**	**24**	**40**

MB - microorganism-binding dressing; SCH - silver-containing hydrofiber dressing

Table II. Age by group and gender

Group	Male (years)	Female (years)	Total (years)
MB	67.2 ± 9.9	71.2 ± 14	69.4 ± 12.2
SCH	64.3 ±10.9	72.5 ± 16.7	69.7 ± 15.2
TOTAL	65.9 ± 10.1	71.9 ± 15.2	**69.5 ± 13.6**

MB - microorganism-binding dressing; SCH - silver-containing hydrofiber dressing

managed through the use of well-established protocols including appropriate wound management, dressings and compression.

For the proportion of ulcers that do not respond to standard care, a multidisciplinary team approach, which must include a vascular surgeon and a plastic surgeon, is required.[17] Other therapeutic alternatives need to be considered to increase the probability of healing. Skin grafting is one of these alternatives.

Using the technique proposed by Levine et al.,[18] Bill et al.[19] quantified bacterial loads in 38 non-healing wounds without classical signs of infection. Tissue biopsy showed >10^5 bacteria/g in 28 of the biospied wounds. Of those identified, the quantitative swab technique detected 79% of the infected wounds. The quantitative information allowed modification of the management plan, resulting in wound healing.

Our findings of the bacteria present are similar to those reported by Gjødsbøl et al.[20] who found that chronic wounds are colonised by multiple bacterial species (aerobic and anaerobic), and that once bacteria are established many of them persist within the wound.

A problem with quantitative bacterial cultures (biopsy or swab) is that it may take up to 48 hours to obtain a result, after the decision to graft is typically made. As a result, this methodology is most commonly applied to research. The clinical reality is that surgeons must trust their knowledge and frequently take a more aggressive approach to make sure that the wound bed is clinically 'clean' before grafting.

Another problem with methods in quantitative bacteriology is the difficulty to detect or the underestimation of hard-to-cultivate bacteria. Traditional quantitative methods are limited when determining a threshold value for bacterial bioburden, mainly because *in vitro* growth is needed, and they can only detect viable and cultivable bacteria. A potential solution to this problem may be the panbacterial real-time polymerase chain reaction (RT-PCR), which can quickly determine bacterial loads and provides more precise data on bacteria species.

However, RT-PCR requires specific reagents for each bacterial species. However, the development of a 'Universal' reagent based on the 16S-rRNA gene (a prokaryotic rRNA found in all bacteria), which has a stable structure that changes little over time, allows a quick determination of total bacterial burden with high sensitivity and the detection of both aerobic and anaerobic bacteria.

Gentili et al.[21] published the results of a 4-week clinical evaluation in 19 patients (20 wounds) presenting hard-to-heal vascular leg ulcers, treated with Sorbact dressings. The results showed that the dress-

Table III. Average surface by group and ulcer type

Group	Mean surface (cm^2)		
	Venous	Arterial	Both
MB	42.6	72.0	50.0
SCH	42.9	74.0	50.7

MB - microorganism-binding dressing; SCH - silver-containing hydrofiber dressing

Table IV. Average duration by group and ulcer type

Group	Mean duration (months)		
	Venous	Arterial	Both
MB	34.4	26.4	32.4
SCH	33.5	26.4	31.7

MB - microorganism-binding dressing; SCH - silver-containing hydrofiber dressing

Fig 1. Comparison of bacterial loads at day 0 and day 4

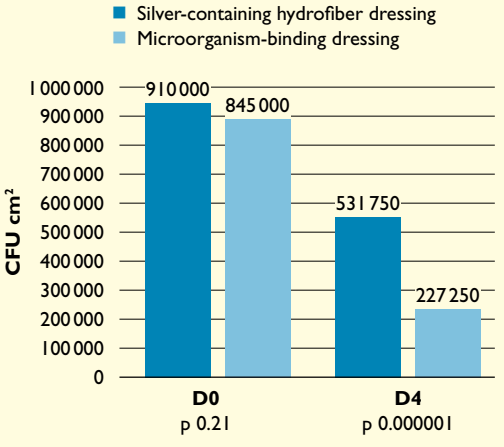
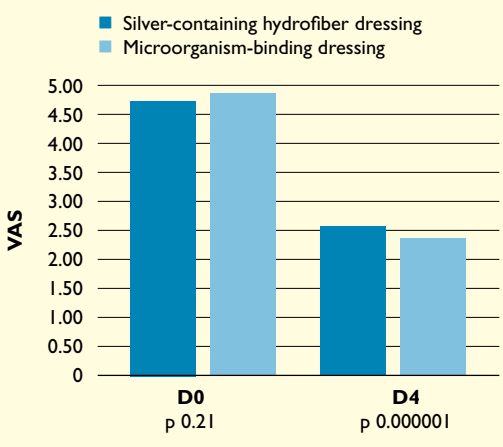


Fig 2. Comparison of pain scores at day 0 and day 4



ing promoted healing in 7 patients and improvement in another 8. They used quantitative 16S RT-PCR to assess bacterial loads. The initial bacterial load was considerably different in the samples ranging from 4.38 x 10^3–2.44 x 10^8 bacterial genomes/mg of tissue. Nevertheless, the average of the total bacterial load before the treatment was 4.41 x 10^7/mg of tissue, which decreased to 1.73 x 10^5/mg of tissue, corresponding to a significant 254-fold decrease in the total bacterial load in the healing wounds, whereas in the non-healing wounds they found only a non-significant 5.3-fold decrease of the total bacterial load. The results allowed them to confirm the suitability of 16S RT-PCR quantification of total bacterial load as a quick and sensitive parameter of wound evolution when performed on tissue biopsies.

When designing our pilot study protocol, we took into consideration the available experimental data about the technology on which the MB dressing is based.[15,22–25] The dressings mechanism of action constitutes a paradox: microorganisms are trapped not destroyed, and eliminated from the wound at dressing change. The mesh structure allows conformability and ease of application. Because of their mechanism of action, it is unlikely that MB dressings will cause bacterial resistance or have systemic absorption and local or systemic toxicity. As bacteria are removed intact, the release of bacterial endotoxins is prevented and the local inflammatory response is reduced. However, a change in the current assumptions about antimicrobial dressings is required to accept that local antimicrobial activity is achieved without using more conventional antimicrobial substances.

In general, the frequency of dressing change depends on the quantity of wound exudate, the wound status and bioburden. For all our patients with these types of wounds, included or not in this study, we change the dressings every day. This is based on the following reasons:

- To assess the wound on a daily basis
- Our belief that a daily change could have a better impact on the preoperative preparation of the wound bed as it could provide a more intense antimicrobial effect
- The fact that the preparation period is short
- MB dressings are indicated to be changed daily.

It is important to highlight the observed pain reduction, which was probably due to a reduction of bacterial load and inflammation as a direct result of the dressings and compression. The presence of silver could be seen as a cause for stronger pain in the SCH group; however, the results didn't show any significant difference between the two groups.

Limitations and future studies

By definition, pilot studies are size-limited and our trial is not an exception. New technologies are not always easy to assess, and in the absence of reliable evidence, pilot studies are a good way to obtain baseline data to assist the designing of further research. A further larger trial is necessary to confirm our data.

Blinding of treatment does not apply to this study. Devices used during a comparative trial are expected to perform similar actions, but as both dressings are physically different, blinding is not possible. What could have been blinded here were the initial assessment of the wound and the assessment of outcomes by different expert clinicians. However, implementing this type of blinding during the present trial was logistically difficult because of the short observation period. A complete analysis about blinding in wound research can be found in a document published by the EWMA's Patients Outcome Group.[26]

This study may also be limited by the swabbing of the wound for bacteria. Although qualitative biopsies are more reliable, they are also more invasive. Hence, we chose to swab the wound area carefully in the same place with the same method.

The observation period was limited to 4 days as a direct result of our protocol of care, which we have adapted for this type of patients. The four-day period is intended to prepare the wound for surgery. Owing to the short duration of the study, we did not record data on ulcer development and healing rates. It is highly likely that by increasing the chance of the graft taking we are improving healing outcomes. However, we focused this pilot study on bacterial loads to investigate the dressings' antimicrobial efficacy.

There are limitations around the identification of the bacterial species, which are due to the traditional culture methods we used. As RT-PCR becomes increasingly accessible and widely used, more clinical evidence will be available, and it is highly likely that the bacteriological criteria for wound infection that we apply today will be challenged and modified in the future.

Conclusions

Our evaluation seems to confirm that, independently from their mechanisms of action, MB dressings as well as SCH dressings are both effective in reducing bacterial burden in critically colonised or locally infected chronic venous leg ulcers without inducing adverse events.

In this pilot trial, MB dressings were significantly more effective in reducing bacterial numbers than SCH dressings. However, the size of the population, represents a challenge regarding comparative efficacy. A trial including a larger population, a longer follow up and the use of PCR techniques for quantitative bacteriology are required to confirm these results. ■

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Dialkylcarbamoyl chloride-impregnated dressing for the prevention of surgical site infection in women undergoing cesarean section: a pilot study

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Abstract

Introduction: Incisional surgical site infections (SSIs) occur in approximately 1.8–9.2% of patients undergoing cesarean section (CS) and contribute to prolonged hospitalization time and increased treatment costs. Dressings impregnated with dialkylcarbamoyl chloride (DACC) are an innovative approach to wound treatment based on a solely physical mechanism of action, and therefore can be used safely and without time restrictions in women during the puerperal and lactation period.

Material and methods: A single-blinded randomized, controlled pilot study was conducted at the Mazovian Bródno Hospital, a tertiary care hospital, between December 2013 and March 2014, and it evaluated the presence of superficial and deep SSIs in patients during the first 14 days after a CS. Patients were randomly allocated to receive treatment with either a DACC dressing or a standard surgical dressing.

Results: One hundred and forty-two patients after planned or emergency CS were enrolled in the study. No significant differences between the groups were observed with regard to patients' basic demographic and perioperative characteristics. The rate of superficial and deep SSIs was 2.8% in the group of patients who received a DACC dressing compared to 9.8% in the group with a standard surgical dressing (p = 0.08). Patients with SSIs who received a standard surgical dressing required systemic antibiotic therapy significantly more frequently (p = 0.03). Based on the logistic regression model developed, the pre-pregnancy body mass index was the only statistically significant risk factor for SSI (p = 0.015).

Conclusions: The results of the pilot study indicate a decreasing tendency of the SSI rate in patients after a CS who received DACC impregnated dressings.

Key words: dialkylcarbamoyl chloride, surgical site infection, cesarean section.

Introduction

A rapid increase in the rate of cesarean sections (CS) observed within the last 30 years, especially in developed countries, has resulted in the fact that currently it is one of the most frequently performed surgical procedures. According to the literature data and depending on the region of the world, 0.4–40.5% of all deliveries have a surgical outcome [1]. Incisional wound infection defined according to the Centers for Disease Control and Prevention (CDC) criteria as a superficial or deep surgical site

infection occurs in approximately 1.8–9.2% of patients after a CS, being one of the most common complications that may lead to wound dehiscence or systemic infections in case of lack of sufficient prophylaxis or inappropriate treatment [2–8]. Increased morbidity, prolonged hospitalization time, increased rate of hospital readmissions and growing treatment costs are all consequences of the above [9].

Dressings impregnated with dialkylcarbamoyl chloride (DACC) are an innovative approach used in the treatment of venous, arterial, diabetic and pressure ulcers, burns, post-traumatic and post-operative wounds [10–13]. Dialkylcarbamoyl chloride, a hydrophobic derivative of fatty acids, irreversibly binds microorganisms as a result of an interaction between hydrophobic particles in the presence of the aqueous medium, therefore allowing for elimination of bacteria and fungi during dressing replacement. The mechanism of action is based on the fact that the majority of pathogens isolated from infected wounds express high to moderate cell surface hydrophobicity (CSH), which on the one hand enables cell attachment and infection initiation by microbes, but on the other hand facilitates their aggregation on the surface of a hydrophobic dressing under moist wound conditions [14–17]. As a result, the number of pathogenic microorganisms in the wound bed is significantly reduced, and their proliferation as well as toxin production is limited [18, 19]. Additionally, the results of recently published *in vitro* studies demonstrated a separate mechanism of action present within hydrophobic dressings, responsible for accelerated wound healing, namely stimulation of fibroblast proliferation and migration [20]. Due to the fact that dressings have a solely physical mechanism of action that is not accompanied by a release of additional antimicrobial substances, the risk of cytotoxicity and sensitization has been eliminated and there are no risks associated with resistance development among bacteria and fungi responsible for wound infections. As a result, hydrophobic dressings can be used safely and without time restrictions, including in women during the puerperal and lactation period.

Taking into account the continuously increasing number of CS and a wide spread of factors responsible for wound healing disturbances in the population of women of reproductive age, such as obesity, diabetes and nicotinism, it is necessary to search for new, more effective methods to prevent infections of surgical wounds.

This study aimed to assess the efficacy of dressings impregnated with DACC in the prevention of incisional surgical site infections in patients undergoing cesarean section.

Material and methods

A single-blinded randomized, controlled pilot study was conducted at the Department of Obstetrics, Gynecology and Oncology, Mazovian Bródno Hospital, Warsaw, Poland between December 2013 and March 2014. Mazovian Bródno Hospital is a tertiary care and academic hospital for the Medical University of Warsaw, performing approximately 1300 deliveries per year, with the CS rate of 51.8% in the study period. Expedited approval for this study was obtained from the Ethics Committee at the Medical University of Warsaw, and written informed consent was gained from all participants. Patients after a planned or emergency CS were enrolled in the study. The inclusion criteria were as follows: age above 18 years, single or multiple pregnancy, mental and physical capability to provide written consent for participation in a clinical trial, and patient's declared compliance with the study plan. Women less than 18 years old or unable to give informed consent were excluded from the study. Patients were randomized into 2 groups depending on the dressing that had been applied. Patients in whom after a cesarean section a dressing impregnated with DACC (Sorbact Surgical Dressing, ABIGO Medical AB, Sweden) was used constituted the study group, whereas patients who received a standard surgical dressing were included in the control group. Simple randomization with the 1 : 1 allocation ratio performed by an operating theater nurse was used to alternate patients enrolled for alternate dressings – even number: DACC-impregnated dressing; odd number: standard surgical dressing.

Data on patient characteristics, pre-, peri- and postoperative course were taken from hospital medical records. The analysis included age, race, parity, pre-pregnancy weight, weight gain during pregnancy, pre-pregnancy body mass index (BMI), gestational age, history of pre-gestational or gestational diabetes mellitus, chronic or pregnancy-induced hypertension, previous CS, tobacco use during pregnancy, mode of CS (planned/emergency), duration of surgery, surgeon experience, hemoglobin levels prior to and 24 h after surgery, and hospitalization time after surgery. An emergency CS was defined based on the time between a decision and skin incision below 30 min. The surgery time was measured between skin incision and skin closure. The hospitalization time after surgery was the number of days from the CS (day 0) to the patient's discharge from hospital. The surgeon's experience was determined based on the medical position and work experience, and classification to one of three groups was performed: resident – a medical doctor during specialization in obstetrics, an obstetrics specialist working for 5 years at most, or an obstetrics specialist working for more than 5 years.

In all patients enrolled in the study a transverse skin incision (Pfannenstiel) followed by a transverse uterine incision in its lower segment was applied. For fascial, subcutaneous tissue and skin incision closure, continuous antibacterial braided absorbable suture (Vicryl Plus 1, Ethicon, USA), single monofilament absorbable suture (Monosyn 2/0, B. Braun Melsungen AG, Germany) and subcuticular continuous monofilament non-absorbable suture (Prolene 2-0, Ethicon, USA), respectively, were used. All participants received an intravenous antibiotic dose as prophylaxis – 1 g of cefazolin 0–30 min prior to the start of surgery. Additionally, in all patients wound irrigation with an octenidine solution (Octenisept, Schülke & Mayr GmbH, Germany) was performed prior to the closure of subcutaneous tissue. The surgical team was blinded to the dressing type until skin closure.

Pursuant to the valid study protocol, in all subjects dressings remained in situ for the first 48 h after surgery unless there were reasons for dressing replacement such as excessive wound bleeding and/or dressing detachment. After 48 h dressings were removed in both groups, and the first clinical wound evaluation was performed. According to the management strategy at the clinic, patients were discharged on the third day after surgery and were recommended to re-visit on day 7 in order to have skin suture removed. The second clinical wound assessment was performed at this visit. The third and final wound evaluation was scheduled on day 14 after a CS. On the discharge day all patients for whom less than 14 days had passed since surgery received detailed instructions regarding surgical site infections (SSIs) and were informed about the need to report at hospital in case at least one of the following symptoms was observed: fever, suppurative secretion from the surgical site, redness, edema, warmth, pain or tenderness of the surgical site area. Patients who did not report for follow-up visits 7 and 14 days after a CS were excluded from the final analysis.

At each surgical wound evaluation scheduled in the study, symptoms of superficial or deep SSI were analyzed according to the CDC criteria [2]. Additionally, the presence of surgical wound dehiscence, defined as separation of the skin, subcutaneous tissue and/or fascia resulting from an incisional SSI, was evaluated. Other parameters subject to the analysis in the group of patients with wound infection were as follows: time of wound infection occurrence (defined as the period from day 0 to the day when first infection symptoms developed), need for systemic antibiotic treatment, need for hospital readmission and need for a surgical intervention. All surgical wound evaluations during patient hospital stay, follow-up visits and self-referral to hospital, as well as SSI classification according to the CDC criteria, were performed by one of the authors (PS).

From all patients with clinical symptoms of SSI, wound swabs were collected in order to perform a microbiological analysis and to identify the responsible pathogen (Copan Sterile Transport Swab, Copan Diagnostics, USA).

CONSORT 2010 guidelines for randomized controlled trials including a checklist and flow diagram were applied to ensure the quality of the conducted study [21].

Statistical analysis

The primary outcome in this study was development of superficial or deep SSI within the first 14 days after a CS. In order to assess whether individual pre-, peri- and post-operative variables affect the development of surgical site infection in women undergoing CS, a logistic regression model with forward selection was designed. The model included the following variables: age, race, parity, gestational age, pre-pregnancy weight, weight gain during pregnancy, pre-pregnancy BMI, pre-gestational or gestational diabetes mellitus, chronic or pregnancy-induced hypertension, previous CS, tobacco use during pregnancy, mode of CS, duration of surgery, surgeon experience, hemoglobin levels prior to and 24 h after surgery, hospitalization time after surgery as well as dressing type.

A statistical analysis was performed using SPSS 17.0 for Windows software (SPSS Inc, Chicago, IL). The Shapiro-Wilk test was used for a normality analysis. Continuous variables were compared by the *t* test, or the Mann-Whitney *U* test, as appropriate. For categorical variables the χ^2 test or the Fisher exact test were applied. Statistical significance was set at $p < 0.05$.

Results

In the period between December 2013 and March 2014 at the Department of Obstetrics, Gynecology and Oncology 193 patients underwent CS, and 31 of them did not meet the study inclusion criteria. One hundred and sixty-two participants were randomized, however 20 women (10 in each group) did not report for scheduled follow-up visits and were excluded from the analysis, leaving a total of 142 eligible patients. The number of participants evaluable for final analysis was equal in both groups – 71 patients in the group with a DACC-impregnated dressing (study group) and in the group with a standard surgical dressing (control group). The patient recruitment process and randomization are summarized in the CONSORT 2010 flow diagram (Figure 1).

Eighteen (25.3%) patients in the study group and 17 (23.9%) patients in the control required

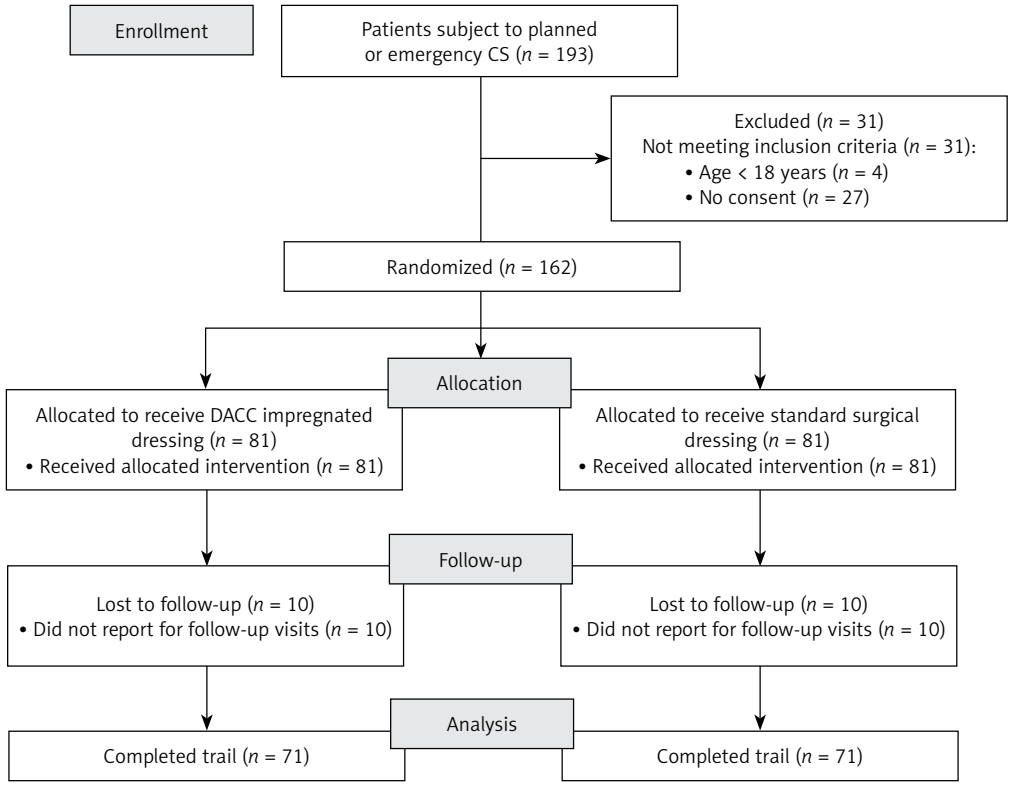

Figure 1. CONSORT 2010 flow diagram of the recruitment process and randomization

CS – cesarean section, DACC – dialkylcarbamoyl chloride.

dressing replacement within the first 48 h following surgery as a result of wound hemorrhage (p = 0.84). There were no cases of dressing detachment in both groups.

Demographic, peri- and postoperative characteristics are shown in Table I. There were no significant differences between the two groups.

Primary and secondary study outcomes are summarized in Table II. The rate of surgical site infections in the group with a DACC-impregnated dressing was 2.8% (2 cases of superficial SSI), whereas in the group with a standard surgical dressing it was 9.8% (6 cases of superficial and 1 case of deep SSI) (p = 0.08). One (1.4%) patient in the control group developed surgical wound dehiscence due to infection. The same patient required rehospitalization and a surgical intervention due to necrotizing fasciitis. In the study group there were no cases of wound dehiscence, and none of the patients who received a DACC-impregnated dressing required hospital readmission and/or surgical intervention. In 5 (7.0%) cases of wound infection in the control group systemic antibiotic treatment was instituted, whereas it was not necessary in the study group (p = 0.03). The mean time to first symptoms of wound infection was 10.5 and 8.8 days in the study and control group, respectively (p = 0.24).

The microbiological analysis of cultures from infected wounds demonstrated *Staphylococcus epidermidis* in 2 and 3 cases of SSIs in the study and control group, respectively. In the remaining patients in the control group wound infection was caused by *Pseudomonas aeruginosa* (2×), *Streptococcus* sp. (1×) and methicillin-resistant *S. epidermidis* (1×).

The logistic regression model used to determine the effects of selected parameters on SSI development was statistically significant ($\chi^2(1) = 5.52$; p = 0.019) and explained 10.1% of observed variance for the dependent variable (R^2 Nagelkerke = 0.101). The Hosmer-Lemeshow test demonstrated that the model is appropriate for data collected: $\chi^2(8) = 6.13$; p = 0.632. According to the logistic regression analysis, only the pre-pregnancy BMI was a significant predictor of wound infection (B = 0.13; W = 5.96; p = 0.015; exp(B) = 1.139; 95% CI: 1.026–1.265).

Discussion

This study aimed to assess the efficacy of dressings impregnated with DACC in the prevention of wound infection in patients after a CS. To our knowledge there have not been any studies published to date on the use of such dressings in the prevention of surgical wound infection. The re-

Table I. Demographic, peri- and postoperative characteristics

Parameter	Study group (n = 71)	Control group (n = 71)	P-value
Age [years]	30.9 ±4.5 (19–41)	31.2 ±5.1 (19–43)	0.64
Race:			> 0.999
Caucasian	70 (98.6)	71 (100)	
Non-Caucasian	1 (1.4)	0 (0)	
Pre-pregnancy weight [kg]	67.3 ±12.4 (48–116)	68.8 ±16.9 (48–116)	0.78
Weight gained during pregnancy [kg]	14.4 ±5.6 (0–27)	13.3 ±5.6 (3–30)	0.26
Pre-pregnancy BMI [kg/m²]:	24.3 ±4.1	25.3 ± 6.0	0.77
< 25	44 (62.0)	41 (57.8)	0.61
≥ 25 and < 30	18 (25.3)	17 (23.9)	0.84
≥ 30 and < 40	9 (12.7)	10 (14.1)	> 0.999
≥ 40	0 (0)	3 (4.2)	0.24
Parity:			
Nulliparous	24 (33.8)	34 (47.9)	0.09
Gestational age [weeks]	37.9 ±2.7 (24–41)	38.2 ±2.2 (28–41)	0.45
Diabetes mellitus:	7 (9.8)	7 (9.8)	> 0.999
PGDM	2 (2.8)	4 (5.6)	0.68
GDM	5 (7.0)	3 (4.2)	0.72
Hypertension:	7 (9.8)	7 (9.8)	> 0.999
Pre-pregnancy HTN	1 (1.4)	3 (4.2)	0.62
PIH	6 (8.4)	4 (5.6)	0.74
Tobacco use during pregnancy	4 (5.6)	5 (7.0)	> 0.999
Mode of CS:			
Planned	53 (74.7)	51 (71.8)	0.70
Emergency	18 (25.3)	20 (28.2)	0.70
Previous CS	19 (26.8)	17 (23.9)	0.70
Duration of surgery [min]	37.2 ±8.0 (21–57)	35.3 ±12.7 (17–105)	0.06
Surgeon experience:			
Resident	32 (45.1)	29 (40.9)	0.61
Specialist ≤ 5 years	16 (22.5)	16 (22.5)	> 0.999
Specialist > 5 years	23 (32.4)	26 (36.6)	0.60
Pre-operative hemoglobin [g/dl]	12.1 ±0.9 (9.8–14.1)	12.0 ±1.0 (9.4–14.0)	0.68
Post-operative hemoglobin [g/dl]	10.7 ±1.2 (7.6–13.5)	10.7 ±1.1 (8.0–12.7)	0.64
Median (range) time of post-operative hospital stay [days]	4.4 ±2.3 (3–15)	4.5 ±2.5 (3–17)	0.59

Data are expressed as mean ± SD/(range) or as frequency (%). BMI – body mass index, PGDM – pre-gestational diabetes mellitus, GDM – gestational diabetes mellitus, HTN – hypertension, PIH – pregnancy-induced hypertension, CS – cesarean section.

sults of the pilot study indicated a decreasing tendency of the observed surgical site infection rate in patients who received DACC dressings. However, when the results obtained were compared to a standard surgical dressing, statistical significance was not achieved, and in order to draw final conclusions it is necessary to perform studies in a larger group of patients. From the point of view of health-care system economics and cost reduction, in the study group there were no

Table II. Primary and secondary outcomes

Parameter	Study group (n = 71)	Control group (n = 71)	P-value
No. of patients with SSI (%)	2 (2.8)	7 (9.8)	0.08
No. of patients with SSI and wound dehiscence (%)	0 (0)	1 (1.4)	0.50
No. of patients with SSI who required systemic antibiotic treatment (%)	0 (0)	5 (7.0)	0.03
No. of patients with SSI who required hospital readmission (%)	0 (0)	1 (1.4)	0.50
No. of patients with SSI who required surgical intervention (%)	0 (0)	1 (1.4)	0.50
Median (range) time of SSI occurrence [days]	Study group (n = 2)	Control group (n = 7)	
	10.5 (10–11)	8.8 (6–13)	0.24

Data are expressed as frequency (%). SSI – surgical site infection.

cases of surgical wound dehiscence and none of the patients required rehospitalization or surgical intervention. Additionally, patients in whom a hydrophobic dressing was applied required systemic antibiotic therapy significantly less frequently. As a result, the use of hydrophobic dressings in standard management strategies for wounds in patients undergoing a CS may contribute to reduced total costs of treatment.

The observed incidence of wound infection after a CS, namely 2.8% or 9.8% depending on the type of dressing used, is similar to results observed by other authors [3–8]. The obtained results probably do not reflect the total SSIs rate due to the fact that the analysis was limited to superficial and deep infections without the organ/space group, and there was a 14-day follow-up after surgery, contrary to the recommended 30-day period presented in the CDC criteria [2]. Introduced changes were a result of the assumption that the rate of organ/space SSI after a CS is low, and dressings have an insignificant effect on their occurrence. The fact that within the scheduled 2 weeks of a follow-up wound infection diagnosis was performed only by a trained healthcare provider also was of importance. Our assumptions are supported by literature data reporting that superficial and deep wound infections after a CS constitute 93–100% of all SSIs, and 77–95% of them develop within the first 14 days after the surgery [4–7]. In order to provide additional verification of the results, a hospital medical database was analyzed to search for patients referred to an outpatient clinic with symptoms suggesting SSIs, and in whom the period since the surgery ranged between 15 and 30 days. There were no records corresponding to such criteria. At the same time, the study by Whitby *et al.* demonstrated a high negative predictive value of patient wound self-monitoring exceeding 97%, in case of lack of infection symptoms and irrespective of the patient knowledge regarding SSIs [22]. There is a slight likelihood of an error of verification performed, however, as patients might have reported to another medical centre.

According to the analysis of risk factors for surgical wound infections, only pre-pregnancy BMI was a statistically significant variable. The fact that obesity increases the risk of wound infection after a CS has been confirmed by many publications [5–8]. It is presumed that excessive thickness of the subcutaneous tissue favors hypoperfusion of tissues, resulting in their ischemia and making antibiotic therapeutic concentration difficult to achieve [23]. An additional aspect is the fact that obesity is often accompanied by carbohydrate metabolism disturbances and prolonged surgery time due to technical difficulties and the need to perform a longer skin incision [23]. It seems that due to a constantly increasing rate of obese or overweight women subject to a CS it is justified to verify and adjust prophylactic doses of antibiotics administered prior to surgery in this group of patients. Supervision by a dietician may also be of importance in the period prior to and during pregnancy.

Lack of confirmed statistical significance for other remaining risk factors for SSIs, such as diabetes, prolonged surgery time, surgeon experience or emergency mode of CS in the present study is probably a result of a too small study group compared to previous publications [5–8].

The microbiological analysis of wound cultures indicated that the main pathogen responsible for infection in both groups is coagulase-negative *Staphylococcus epidermidis*, strains of which exhibit high variability with regard to CSH, and hydrophilicity is more predominant [17, 24–26]. In the group with hydrophobic dressings and in the group with a standard surgical dressing there were no cases of infection caused by *S. aureus*, whereas in the latter group the presence of *Pseudomonas aeruginosa* was confirmed twice. This last phenomenon can be explained by an observed increase in CSH of *P. aeruginosa* in carbon dioxide atmosphere and in the presence of serum [17]. These conditions, similar to the wound en-

vironment under an occlusive dressing, may contribute to increased absorption of bacteria due to hydrophobic interactions.

In conclusion, it is commonly known that infection impairs and delays wound healing due to damage of healthy cells by toxins released by pathogenic microorganisms and enzymes from inflammatory cells. Only in the case of spreading or systemic infection is it recommended to use antibiotics in combination with topical antimicrobial treatment. However, when only wound contamination or colonization occurs and the healing process progresses, the use of methods as above is not recommended due to systemic action and a possibility of resistance development. Surgical wounds in obstetrics are classified as clean-contaminated wounds; therefore in infection prophylaxis it is recommended to use local methods and preferably those that limit the release of additional antimicrobial agents due to lactation. This study has demonstrated that DACC-impregnated dressings can be applied for the prevention of SSIs in women after a CS based solely on a physical mechanism of action. Taking into account the constantly increasing rate of patients subject to CS, and the fact that a considerable number of women of reproductive age have risk factors for wound infections, further attempts to use such dressings are justified and the obtained study results are promising. The study presented above was preliminary; a randomized, controlled trial with a larger group of patients is ongoing, and its aim is to draw final conclusions.

Conflict of interest

The authors declare no conflict of interest.

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Original Articles

Randomized Controlled Trial Evaluating Dialkylcarbamoyl Chloride Impregnated Dressings for the Prevention of Surgical Site Infections in Adult Women Undergoing Cesarean Section

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Abstract

Background: Surgical site infections (SSI) occur in 1.8%–9.2% of women undergoing cesarean section (CS) and lead to greater morbidity rates and increased treatment costs. The aim of the study was to evaluate the efficacy and cost-effectiveness of dialkylcarbamoyl chloride (DACC) impregnated dressings to prevent SSI in women subject to CS.
Methods: Randomized, controlled trial was conducted at the Mazovian Bródno Hospital, a tertiary care center performing approximately 1300 deliveries per year, between June 2014 and April 2015. Patients were randomly allocated to receive either DACC impregnated dressing or standard surgical dressing (SSD) following skin closure. In order to analyze cost-effectiveness of the selected dressings in the group of patients who developed SSI, the costs of ambulatory visits, additional hospitalization, nursing care, and systemic antibiotic therapy were assessed. Independent risk factors for SSI were determined by multivariable logistic regression.
Results: Five hundred and forty-three women undergoing elective or emergency CS were enrolled. The SSI rates in the DACC and SSD groups were 1.8% and 5.2%, respectively ($p = 0.04$). The total cost of SSI prophylaxis and treatment was greater in the control group as compared with the study group (5775 EUR vs. 1065 EUR, respectively). Independent risk factors for SSI included higher pre-pregnancy body mass index (adjusted odds ratio [aOR] = 1.08; [95% confidence interval [CI]: 1.0–1.2]; $p < 0.05$), smoking in pregnancy (aOR = 5.34; [95% CI: 1.6–15.4]; $p < 0.01$), and SSD application (aOR = 2.94; [95% CI: 1.1–9.3]; $p < 0.05$).
Conclusion: The study confirmed the efficacy and cost-effectiveness of DACC impregnated dressings in SSI prevention among women undergoing CS.

Cesarean section (CS) remains to be one of the most common surgical procedures performed worldwide and available data indicate that surgical interventions constitute approximately 0.4%–40.5% of all deliveries [1]. Depending on the definition and the observational period, surgical site infection (SSI) occurs in about 1.8%–9.8% of all CS patients and leads to greater morbidity rates, prolonged hospitalization, and increased number of hospital readmissions [2–9]. Post-cesarean SSI has been estimated to extend the period of hospitalization by 4 d, and at the same time generating an additional cost of 3716 EUR per patient [9].

A recently published pilot study revealed a downward trend in SSI rates after CS if dialkylcarbamoyl chloride (DACC) impregnated dressings were used as method of post-operative SSI prevention [10]. The characteristic feature of the dressing, whose fibers were covered with a hydrophobic derivate of fatty acids, is its solely physical mechanism of action. It uses the interaction between hydrophobic molecules in the presence of aqueous medium, as well as the fact that the majority of pathogens responsible for the development of SSIs demonstrate moderate to high cell surface hydrophobicity (CSH) [11]. High CSH allows microorganism

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to adhere to cells and to initiate infection, at the same time causing their aggregation on the surface of the impregnated dressing, decreasing both their number in the wound bed and proliferation [12–16]. Described mechanism of action is not associated with the release of additional antimicrobial substances, thus eliminating the risk of cytotoxicity and sensitization, which is particularly important during the periods of puerperium and lactation [16]. To date, the efficacy of DACC-impregnated dressings has been proven in the treatment of venous, arterial and pressure ulcers, burns, diabetic foot, and hard-to-heal post-traumatic and post-operative surgical incisions [17–20].

Taking into consideration the steadily growing CS rates, as well as factors that are responsible for impaired wound healing in women of reproductive age, such as obesity, diabetes mellitus, or smoking, it is vital to search for new, efficient, and safe strategies of preventing obstetric SSI. Also, from the point of view of healthcare system economics, it is important to avoid additional costs, which would allow for a widespread application rather than in high-risk patients only. Therefore, the aim of the study was to evaluate the efficacy and cost-effectiveness of DACC impregnated dressings in the prevention of post-operative SSI among CS women.

Patients and Methods

Setting and study population

The single-blinded, randomized, controlled clinical study was conducted between June 2014 and April 2015 at the Mazovian Bródno Hospital, a tertiary referral center and a clinical hospital of the Medical University of Warsaw. Local Ethics Committee approved of the study (reference no. KB/127/2014 received on June 10, 2014) and written informed consent was obtained from all participants. The trial was registered with ClinicalTrials.gov (reference no. NCT02168023).

The inclusion criteria were: Patient age >18 y, emergency or elective CS, singleton or multiple pregnancy, mental and physical capacity to consent to participation in a clinical trial, CS performed by transverse skin incision followed by a transverse uterine incision in its lower segment, antibiotic prophylaxis administered zero to 30 min before the surgery, and wound irrigation with octenidine solution before subcutaneous tissue closure.

The patients were randomly assigned to two groups, depending on the applied dressing. Patients with DACC impregnated dressing (Sorbact Surgical Dressing®, ABIGO Medical AB, Sweden) constituted the study group, whereas women with standard surgical dressing (SSD) (Tegaderm + Pad®, 3M Health Care, St. Paul, MN) were recruited as control groups. Simple randomization with the 1:1 allocation ratio, conducted by an operating room (OR) nurse, was used to alternate the patients; even number: DACC dressing, and odd number: SSD. For masking purposes, all dressings were placed in white envelopes and sealed. The surgical team was blinded to the type of dressing until skin closure.

Data on patient demographics, peri- and post-operative course were collected from hospital medical records. Demographic parameters included: Age, race, pre-pregnancy weight, weight gain during pregnancy, height, pre-pregnancy body mass index (BMI), parity, gestational age; presence of diabetes mellitus (pre-gestational or gestational diabetes), hypertension (chronic hypertension or pregnancy-induced hypertension); smoking in pregnancy, history of previous CS, and presence of singleton/multiple pregnancy.

Peri- and post-operative parameters included: Type of dressing; mode of CS (emergency, elective); duration of the surgery; surgeon experience (resident, assistant specialist, consultant); type of anesthesia (spinal, general); presence of meconium stained amniotic fluid (MSAF); hemoglobin concentration 24 h before and 24 h after the surgery; receipt of blood transfusion, and length of post-operative hospital stay.

SSI-related parameters included: Presence of superficial or deep SSI during the first 14 d after the surgery, wound dehiscence; onset of the first symptoms of SSI; the need for systemic antibiotic therapy, hospital re-admission and/or re-operation; the number of ambulatory visits; length of additional hospitalization, and identification of the pathogen responsible for SSI.

The technique of a transverse skin incision (Pfannenstiel) followed by a transverse uterine incision in its lower segment was used in all women, as described previously [10]. For subcutaneous tissue and skin incision closure, single monofilament absorbable suture (Monosyn 2/0, B. Braun Melsungen AG, Germany) and subcuticular continuous monofilament non-absorbable suture (Prolene 2-0, Ethicon, Somerville, NJ), were used respectively. All patients received antibiotic prophylaxis (1g of cefazolin) administered zero to 30 min before the surgery according to Polish National Consultants of General Surgery and Clinical Microbiology recommendations and wound irrigation with octenidine solution (Octenisept®, Schülke & Mayr GmbH, Germany) proceeded subcutaneous tissue closure [21]. Octenidine is a cationic, surface active, topical antimicrobial agent with high bactericidal and fungicidal activity, and cytotoxicity similar to that of other common antiseptics such as chlorhexidine [22].

The study plan resembled the one described in the pilot study [10]. Briefly, the dressing was left in situ for the first 48 h post-operatively in all participants, unless there were reasons for replacement, e.g., wound hemorrhage or detachment of the dressing. After that time, the dressing was removed and the first clinical assessment of wound healing was performed. The patients were discharged home on post-operative day three, unless contraindicated, and recommended to revisit on day seven for skin suture removal and second wound evaluation. Third and final wound assessment was scheduled for post-operative day 14. Patients who failed to report for follow-up visits were excluded from the final analysis. Each wound assessment during patient hospitalization, the follow-up visits, or in case of patient's self-referral to an ambulatory center, was performed by one of two authors (PS, MB), blinded to the type of the dressing used.

Study outcome definitions

The symptoms of superficial or deep SSI were analyzed according to the U.S. Centers for Disease Control and Prevention (CDC) criteria [23]. Wound dehiscence was defined as separation of the skin, subcutaneous tissue, or fascia, resulting from infection. Time of primary hospitalization was defined as period from the day of surgery (day zero) to discharge from the hospital. Time of additional hospitalization

was defined as period from the first SSI symptoms to treatment completion and discharge from the hospital (in cases when SSI developed during primary hospitalization and was the main reason for prolonged stay in the hospital), or from day one of re-admission because of SSI until treatment completion and discharge from the hospital (in cases when primary hospitalization was finished). Emergency CS was defined as procedure performed within 30 min of the decision. Surgeon experience was determined on the bases of specialization in obstetrics and years of experience: Resident—physician in specialist training, assistant specialist—specialization in obstetrics for ≤5, consultant—specialization in obstetrics for >5 y.

Cost data analysis and definitions

In case of SSI occurrence, the following costs were analyzed: Systemic antibiotic therapy, ambulatory visits, additional hospitalization, and additional nursing care. The costs were calculated in Polish zloty (PLN) and then converted to Euro (EUR), based on the Polish National Bank exchange rate from June 1, 2015 (1 EUR = 4.1 PLN).

The cost of antibiotic therapy, defined as the cost of therapy from day one to the last day of SSI treatment, was calculated on the basis of antibiotic prices from the central hospital pharmacy and according to the manufacturer's specifications. The cost of ambulatory visit was calculated on the basis of classifying the patients into one of the Diagnosis Related Groups of Polish National Health Fund (DRG: W40), based on the diagnosis from the International Statistical Classification of Diseases and Related Health Problems v.10 (ICD-10-CM; o86.0—infection of obstetric surgical wound; o90.0—disruption of cesarean delivery wound), and the performed procedure, in accordance with the International Classification System for Surgical, Diagnostic and Therapeutic Procedures v.5.22 (ICD-9-CM; 86.28—non-excisional debridement of wound, infection or burn; 93.57—application of another wound dressing). Using the abovementioned data, the cost of a single ambulatory visit was estimated at 54 PLN (13 EUR). The costs of additional hospitalization in SSI patients who required prolonged primary hospitalization or readmission, together with the costs of additional nursing care obtained from the hospital financial office, amounted to 316 PLN (77 EUR) and 173 PLN (42 EUR) per day, respectively.

In order to determine the total costs of prophylaxis and treatment of SSI in both groups, the costs mentioned above were supplemented with the costs of dressings based on mean retail prices: DACC 11.5 PLN (2.8 EUR) and SSD 20 PLN (4.9 EUR).

Statistical analysis

Statistical analysis was performed using the R package v. 3.0.1 (The R Foundation for Statistical Computing, Vienna, Austria). Continuous variables were compared using the Mann-Whitney *U* test. For categorical variables, the χ^2 test or the Fisher exact test were applied. The p-value of <0.05 was considered as statistically significant.

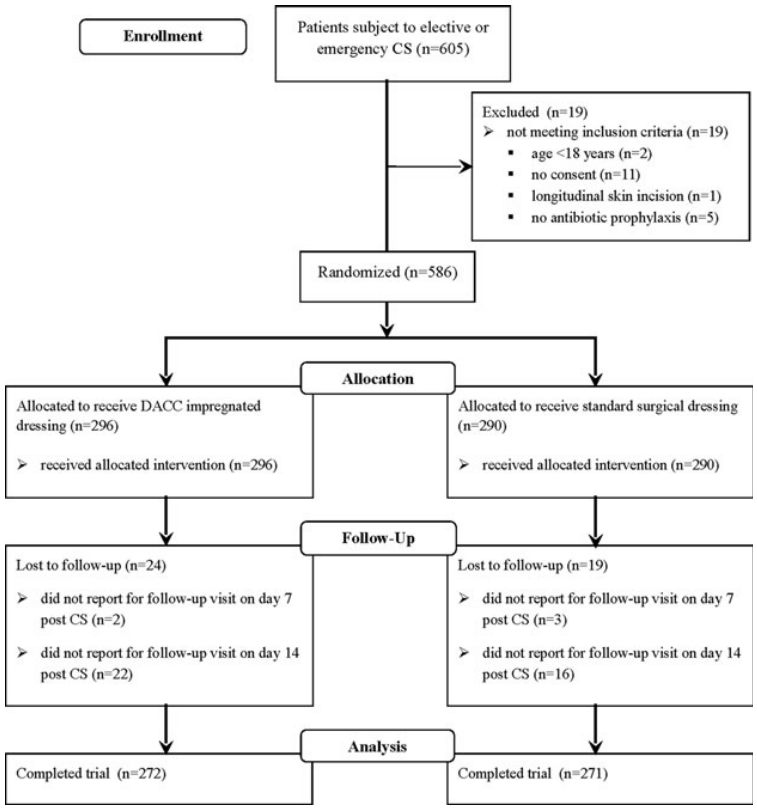

FIG. 1. CONSORT 2010 flow diagram of the recruitment process and randomization. CS, cesarean section; DACC, dialkylcarbamoyl chloride

Table 1. Characteristics of Patients Who Underwent Cesarean Section during the Study Period from June 2014 to April 2015

	Study group (n = *272*)	*Control group* (n = *271*)	*p*
Age (y)	31.2 ± 4.8 (18 – 43)	30.6 ± 4.8 (18 – 44)	.08
≤20	5 (1.8%)	4 (1.5%)	.63
21–30	114 (42.0%)	126 (46.5%)	
31–40	148 (54.4%)	134 (49.4%)	
>40	5 (1.8%)	7 (2.6%)	
Race			
Caucasian	269 (98.9%)	268 (98.9%)	>.999
Non-Caucasian	3 (1.1%)	3 (1.1%)	
Pre-pregnancy weight (kg)	65.8 ± 13.2 (40 –138)	66.4 ± 14.6 (39 –129)	.69
Weight gain during pregnancy (kg)	14.3 ± 6.0 (0 – 40)	14.4 ± 5.6 (0 – 38)	.64
Height (m)	1.66 ± 0.06 (1.48– 1.81)	1.65 ± 0.06 (1.4 – 1.84)	.55
Pre-pregnancy BMI (kg/m^2)	23.9 ± 4.5 (16.3 – 47.7)	24.2 ± 4.9 (14.5 – 43.6)	.57
BMI <25	193 (70.9%)	176 (64.9%)	.31
BMI ≥25 and <30	53 (19.5%)	62 (22.9%)	
BMI ≥30	26 (9.6%)	33 (12.2%)	
Parity			
Primiparous	131 (48.2%)	150 (55.4%)	.11
Multiparous	141 (51.8%)	121 (44.6%)	
Gestational age (wks)	38.1 ± 2.4 (24 – 41)	38 ± 2.5 (24 – 41)	.92
< 37 wks	32 (11.8%)	46 (17.0%)	.11
Diabetes mellitus	26 (9.6%)	35 (12.9%)	.28
PGDM	9 (3.3%)	8 (2.9%)	
GDM	17 (6.3%)	27 (10.0%)	
Hypertension	24 (8.8%)	34 (12.5%)	.08
Pre-pregnancy HTN	11 (4.0%)	8 (2.9%)	
PIH	13 (4.8%)	26 (9.6%)	
Smoking during pregnancy	20 (7.3%)	20 (7.4%)	>.999
Mode of CS			
Elective	214 (78.7%)	211 (77.9%)	.90
Emergency	58 (21.3%)	60 (22.1%)	
Previous CS	96 (35.3%)	87 (32.1%)	.49
Multiple pregnancy	5 (1.8%)	7 (2.6%)	.76
Duration of surgery (min.)	36.3 ± 9.0 (17 – 82)	36.7 ± 11.4 (17 –125)	.94
≤25	35 (12.9%)	34 (12.5%)	.86
25–50	218 (80.1%)	221 (81.5%)	
>50	19 (7.0%)	16 (6.0%)	
Surgeon experience			
Resident	106 (39.0%)	113 (41.7%)	.56
Assistant specialist	73 (26.8%)	77 (28.4%)	
Consultant	93 (34.2%)	81 (29.9%)	
Type of anesthesia			
Spinal	225 (82.7%)	221 (81.6%)	.81
General	47 (17.3%)	50 (18.4%)	
MSAF	20 (7.3%)	21 (7.7%)	.99
Pre-operative Hgb (g/dL)	12.2 ± 1.0 (8.3 – 14.9)	12.3 ± 1.1 (8.7 – 16.1)	.77
Post-operative Hgb (g/dL)	10.9 ± 1.0 (7.1 – 14.2)	11 ± 1.2 (6.5 – 14.6)	.39
Δ Hgb (g/dL)	1.3 ± 0.7 (0.1 – 3.5)	1.3 ± 0.9 (0.1 – 6.5)	.17
Blood transfusion	6 (2.2%)	4 (1.5%)	.75
Length of post-operative hospital stay (d)	4.3 ± 1.9 (3 – 14)	4.6 ± 2.1 (3 – 15)	.22

Data are expressed as mean ± SD/ (range) or as frequency (%).
BMI = body mass index; PGDM = pre-gestational diabetes mellitus; GDM = gestational diabetes mellitus; HTN = hypertension; PIH = pregnancy induced hypertension; CS = cesarean section; MSAF = meconium stained amniotic fluid; Hgb = hemoglobin concentration; Δ Hgb = change in hemoglobin concentration.

In order to identify the factors responsible for post-operative SSI in women after CS, univariate logistic regression, followed by multivariable logistic regression with backward selection based on the Akaike Information Criterion, were performed.

On the basis of the pilot study results, power analysis indicated that a sample size of 248 for each of the two groups was required to detect a difference in SSI proportion, with a power of 90% and $\alpha = 0.05$.

Results

During the study period, between June 2014 and April 2015, there were 1144 deliveries, including 605 cesarean

Table 2. Primary and Secondary Study Outcomes

	Study group (n = 272)	*Control group* (n = 271)	*p*
No. of patients with SSI (%)	5 (1.8)	14 (5.2)	.04
No. of patients with SSI and wound dehiscence (%)	1 (0.4)	2 (0.7)	>.99
No. of patients with SSI who required systemic antibiotic treatment (%)	0	4 (1.5)	.13
No. of patients with SSI who required hospital readmission (%)	0	3 (1.1)	.24
No. of patients with SSI who required surgical intervention (%)	0	0	-
	Study group (n = 5)	*Control group* (n = 14)	
Time of SSI occurrence (d)	7.4 ± 1.14 (6-9)	9.1 ± 3.6 (3–14)	.26
No. of ambulatory visits	4.6 ± 1.67 (2-6)	2.9 ± 1.1 (1– 4)	.02
Length of additional hospitalization (d)	0	8.2 ± 3.2 (5–11)	.22

Data are expressed as mean ± SD/ (range) or as frequency (%)
SSI = surgical site infection.

sections (52.9%), at the Department of Obstetrics, Gynecology and Oncology (Fig. 1). Among the women undergoing CS, 19 failed to meet the inclusion criteria: Two were <18 y of age, 11 were not in the capacity to or failed to consent to participation in the study, one patient had CS performed by a longitudinal skin incision, and five patients did not receive antibiotic prophylaxis. Out of the 586 patients who were deemed eligible for the study and who were randomly assigned into either the DACC group (study group, n = 296) or the SSD group (control group, n = 290), 43 (7.3%) failed to report for follow-up visits and were excluded from further analysis. In the final stage, the study and control groups consisted of 272 and 271 patients, respectively.

Table 3. Microorganisms Isolated from Surgical Site Infections during the Study Period from June 2014 to April 2015

	Study group	*Control group*
Microorganisms	*No. (%)*	*No. (%)*
Enterobacteriaceae	1 (9.1)	9 (56.25)
Klebsiella pneumoniae	0	3
Proteus mirabilis	0	1
Enterobacter cloacae	0	2
Escherichia coli	1	3
Coagulase-positive Staphylococci	2 (18.2)	1 (6.25)
MSSA	2	1
Coagulase-negative Staphylococci	1 (9.1)	1 (6.25)
MSSE	1	0
Staphylococcus hominis	0	1
Anaerobes	2 (18.2)	1 (6.25)
Bacteroides fragilis	1	0
Prevotella bivia	0	1
Peptoniphilus asaccharolyticus	1	0
Enterococcaceae	2 (18.2)	1 (6.25)
Enterococcus faecalis	2	1
Streptococcus sp.	2 (18.2)	0 (0)
Other	1 (9.1)	3 (18.75)
Total	11 (100)	16 (100)

MSSA = methicillin susceptible *Staphylococcus aureus*; MSSE, methicillin susceptible *Staphylococcus epidermidis*

Patient characteristics are presented in Table 1. There were no substantial differences between the DACC and the SSD groups with regard to patient demographics and perioperative course. Surgical site infections were observed substantially more often in the SSD group (Table 2). Incisional SSIs occurred during the first 14 post-operative days in 5.2% of patients from the control group as compared with 1.8% of women from the study group (p = 0.04). No statistically significant differences were found as far as the presence of post-operative wound dehiscence, receipt of systemic antibiotic therapy, or re-admission rates were concerned. Regardless of the fact that women who received the DACC dressing did not require systemic antibiotic therapy and additional hospitalization, the number of ambulatory visits was substantially higher in the study group as compared with the control groups, 4.6 vs. 2.9, respectively (p = 0.02) (Table 2). Mean time of additional hospitalization in the SSD group was 8.2 d. In both groups there were no cases of SSIs in patients with diabetes mellitus, both pre-existing before pregnancy and gestational, and with chronic arterial hypertension. All study participants were HIV-negative.

Enterobacteriaceae, coagulase-positive and negative *staphylococci*, anaerobes, *Enterococcaceae*, and *Streptococcus* sp. were the pathogens responsible for most SSI cases in both groups (Table 3). Microbiological analysis revealed strains of *Enterobacteriaceae* as the dominant group of pathogens isolated in patients from the SSD group, accounting for more than half of the identified microorganisms (56.25%). A similar correspondence was not observed in the DACC group, where *Enterobacteriaceae* constituted 9.1% of the isolated strains, with no dominant group of pathogens.

The univariate analysis revealed pre-pregnancy BMI of $\geq 30\,kg/m^2$ (odds ratio [OR] = 4.5; [95% CI: 1.3–14.8]; p = 0.009), pregnancy induced hypertension (OR = 5.1; [95% CI: 1.4–16.2]; p = 0.008), and smoking in pregnancy (OR = 5.0; [95% CI: 1.3–15.7]; p = 0.009) to be the factors that substantially increase the risk for SSI, and

Table 4. Univariate Analysis of Risk Factors for Surgical Site Infection in Females after Cesarean Section

	No. (%) of patients			
	SSI (n = *19*)	*No SSI* (n = *524*)	*OR (95% CI)*	*p*
Age (y)				
≤30	10 (52.6)	239 (45.6)	1.0	-
31–40	8 (42.1)	274 (52.3)	0.7 (0.23– 2.0)	.48
>40	1 (5.3)	11 (2.1)	2.2 (0.4 –17.9)	.41
Race				
Caucasian	18 (94.7)	519 (99.0)	1.0	-
Non-Caucasian	1 (5.3)	5 (1.0)	5.7 (0.1 –55.2)	.19
Weight gain during pregnancy (kg)				
≤10	7 (37.0)	132 (25.0)	1.0	-
>10	12 (63.0)	392 (75.0)	0.6 (0.2 – 1.8)	.28
Pre-pregnancy BMI (kg/m^2)				
BMI <25	9 (47.4)	360 (68.7)	1.0	-
BMI ≥25 and <30	4 (21.0)	111 (21.2)	0.99 (0.23– 3.2)	>.999
BMI ≥30	6 (31.6)	53 (10.1)	4.5 (1.3 –14.8)	.009
Parity				
Primiparous	14 (73.7)	267 (51.0)	2.7 (0.9 – 9.7)	.06
Gestational age				
< 37 wks	5 (26.3)	73 (13.9)	2.2 (0.6 – 6.7)	.17
Hypertension				
PIH	5 (26.3)	34 (6.5)	5.1 (1.4 –16.2)	.008
Smoking during pregnancy	5 (26.3)	35 (6.7)	5.0 (1.3 –15.7)	.009
Mode of CS				
Elective	13 (68.4)	412 (78.6)	1.0	-
Emergency	6 (31.6)	112 (21.4)	1.7 (0.5 – 4.9)	.27
Previous CS	3 (15.6)	180 (34.4)	0.4 (0.7 – 1.28)	.14
Multiple pregnancy	2 (10.5)	10 (1.9)	6.0 (0.6 –31.6)	.06
Duration of surgery (min.)				
≤25	4 (21.0)	65 (12.4)	1.0	-
>25	15 (79.0)	459 (87.6)	0.53 (0.16– 2.27)	.28
Surgeon experience				
Resident	8 (42.1)	211 (40.3)	1.0	-
Assistant specialist	5 (26.3)	145 (27.7)	0.9 (0.2 – 3.2)	>.999
Consultant	6 (31.6)	168 (32.0)	0.9 (0.3 – 3.2)	>.999
Type of anesthesia				
Spinal	14 (73.7)	432 (82.4)	1.0	-
General	5 (26.3)	92 (17.6)	1.7 (0.5 – 5.1)	.36
MSAF	3 (15.8)	38 (7.2)	2.4 (0.4 – 8.9)	.17
Pre-operative Hgb				
≤12 g/dL	6 (31.6)	191 (36.4)	0.8 (0.2 – 2.3)	.81
Post-operative Hgb				
≤10 g/dL	3 (15.8)	97 (18.5)	0.8 (0.15– 3.0)	>.999
Δ Hgb				
≥3g/dL	1 (5.3)	9 (1.7)	3.2 (0.07–25.1)	.30
Length of post-operative hospital stay (d)				
≤5	13 (68.4)	393 (75.0)	1.0	-
6–10	5 (26.3)	123 (23.5)	1.2 (0.3 – 3.8)	.78
>10	1 (5.3)	8 (1.5)	3.7 (0.08–31.9)	.27
Dressing type				
SSD	14 (73.7)	257 (49.1)	1.0	-
DACC	5 (26.3)	267 (50.9)	0.3 (0.09– 1.03)	.04

SSI = surgical site infection; BMI = body mass index; PIH = pregnancy induced hypertension; CS = cesarean section; MSAF = meconium stained amniotic fluid; Hgb = hemoglobin concentration; Δ Hgb = change in hemoglobin concentration; SSD = standard surgical dressing; DACC = dialkylcarbamoyl chloride-impregnated dressing; CI = confidence interval; OR = odds ratio.

application of the DACC impregnated dressing as the factor that lowers the risk (OR =0.3; [95% CI: 0.09–1.03]; p = 0.04) (Table 4).

In order to identify independent risk factors for SSI, a separate multivariable logistic regression with backward selection was performed. The following parameters were found to influence the risk for SSI: Pre-pregnancy BMI (aOR = 1.08; [95% CI: 1.0–1.2]; $p < 0.05$), smoking in pregnancy (aOR = 5.34; [95% CI: 1.6–15.4]; $p < 0.01$) and SSD application (aOR = 2.94; [95% CI: 1.1–9.3]; $p < 0.05$).

Total estimated cost of SSI prophylaxis and treatment was greater in the control group as compared with the study

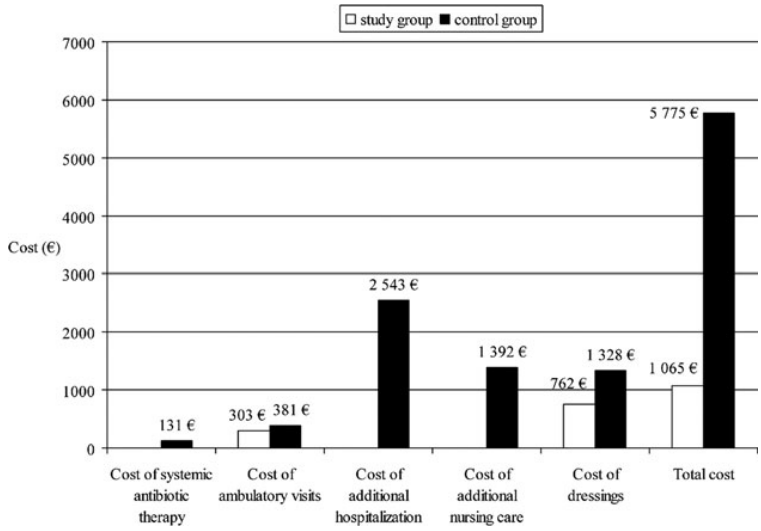

FIG. 2. Cost of treatment attributable to surgical site infection after cesarean section by dressing type.

group, and amounted to 5775 EUR vs. 1065 EUR, respectively (Fig. 2). In the study group it comprised only the cost of ambulatory visits, whereas in the control group total cost encompassed additional expenses because of prolonged hospitalization and additional nursing care. Similarly, systemic antibiotic treatment with metronidazole, cefuroxime, ceftriaxone, amoxicillin, ciprofloxacin, or gentamicin used alone or in combination was necessary only in patients in the control group.

Discussion

The presented study was a single-center, randomized controlled trial, aiming to evaluate the efficacy of DACC impregnated dressings to prevent SSI in women after CS. To the best of our knowledge, it has been the first prospective study on the use of DACC dressings in a large cohort of pregnant women.

Our results confirmed effectiveness of the DACC dressings in SSI prevention after CS. Application of the hydrophobic dressing resulted in a decreased rate of SSI and its considerably milder course, with no need for systemic antibiotic therapy and hospital readmissions. As a consequence, the total cost of SSI treatment was lower in the DACC group and was a result of ambulatory visits only. Despite the fact that the total number of the ambulatory visits was substantially higher in the study group, the dominant element in the total treatment cost was the length of additional hospitalization, with mean duration of 8 d in the group with SSD.

Multivariable logistic regression analysis revealed obesity, smoking, and the use of a standard occlusive dressing as the three independent factors that increase the risk for incisional SSI after CS. The adverse effects of the first two factors have been well-documented in the literature [2,3,5,7,8]. In case of obesity, excessive thickness of subcutaneous tissue is believed to cause tissue hypoperfusion and hypoxygenation, impeding the healing process and antibiotic penetration [24]. The risk of SSI is often additionally increased by the presence of hyperglycemia, prolonged surgery time because of technical difficulties, the need for a longer skin incision, and more blood loss. Also, proper wound hygiene and care may be hampered by the location of the incision between skin folds, what may predispose to the development of infection. As far as smoking is concerned, the components of tobacco smoke cause tissue hypoxia, impair the function of inflammatory cells, and limit fibroblast proliferation and migration, thus delaying wound healing [25–27].

The type of dressing used in prevention of SSI after obstetric operations is of the utmost importance from the point of view of the study goals. Similarly to subcutaneous drains or surgical staples used for skin closure, the type of the applied dressing may affect the risk of SSI [2,5]. Obtained results revealed an almost three-fold increase of SSI risk in patients who received the SSD.

Microorganisms responsible for SSI were similar in both groups, with the exception of more numerous *Enterobacteriacae* strains found among the control groups, which may be explained by the fact that approximately 25% of *Enterobacter* spp. strains isolated from surgical incisions are characterized by high CSH, whereas hydrophobic properties are found in 88% of the *Enterobacter cloacae* strains alone [28]. In case of *Klebsiella pneumoniae*, CSH is affected by the presence of O-antigen lipopolysaccharide or polysaccharide capsule, making bacteria more hydrophilic and, as a result, less susceptible to adhesion to the hydrophobic surface of the dressing [29]. Neither the abovementioned properties of bacterial strains nor the effect of the remaining factors on the CSH of the isolated pathogens were the subject of the investigation. It has been proven that the use of octenidine solution, just as bacterial culture in carbon dioxide atmosphere in the presence of serum, resembling wound conditions under an occlusive dressing, increase CSH, contrary to antibiotics used in pre-operative prophylaxis [11,16,30].

Our study is subject to several limitations, including the fact that the effectiveness of the impregnated dressings was analyzed in a group of women undergoing CS, which, unlike most surgical patients, constitute young population with few comorbidities. Also, the observed SSI incidence after CS

most probably does not reflect the total SSI rate because of the fact that analysis included only superficial and deep SSI, as well as shorter than recommended by the CDC period of observation. Exclusion of organ/space SSI from the analysis was imposed by the fact that the effect of the dressing on the incidence of such infections after CS is limited and the shortened time of the observation, from the recommended 30 d to 14 d, was conditioned by lack of the possibility of effective medical supervision and low patient compliance after that time, as described by Wilson et al. [4]. At the same time, the literature reports indicate that superficial and deep SSIs account for 93%–100% of all cases of SSI following CS, with 78%–100% occurring within 14 d of the surgery [2–4,6,7]. As the subject of the study included only superficial and deep SSI such risk factors as number of vaginal examinations, duration of labor or pre-term rupture of membranes were not included in the analysis, taking into account their correlation with organ/space infections.

To conclude, the use of a DACC-coated dressing decreased the SSI rates among patients after CS and proved its cost-efficacy. Weight reduction before conception, abstaining from smoking in pregnancy, and application of dressings that are effective in SSI prophylaxis, are the key factors which might prevent SSIs after CS.

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Author Disclosure Statement

All authors report no conflicts of interest relevant to this article.

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