

TITLE PAGE

Title: *Dialkylcarbamoyl chloride dressings in the prevention of surgical site infections following non-implant vascular surgery*

Authors:

Nelson Bua¹, George E Smith¹, Joshua P Totty¹, Daniel Pan¹, Tom Wallace¹, Daniel Carradice¹, and Ian C Chetter¹

Institution:

¹Academic Vascular Surgical Unit, Hull York Medical School, UK

Corresponding author:

Joshua P Totty

Academic Vascular Surgical Unit, Hull Royal Infirmary, Anlaby Road, Hull, HU3 2JZ

Email: Joshua.totty@hyms.ac.uk

Tel: (+44) 01482674643

Funding: No external funding

Category: Original Article

Previously not published / presented

Abstract:

Background: Dressings coated with Dialkylcarbamoyl chloride (DACC) are highly hydrophobic and irreversibly bind multiple types of bacteria, trapping them in the dressing and reducing the number of organisms at the wound surface. We aimed to assess the impact of DACC coated postoperative dressings on the incidence of surgical site infection (SSI) in non-implant vascular surgery patients.

Methods: Two hundred patients undergoing non implant vascular surgery were prospectively recruited at a single vascular centre. The initial 100 patients had their operative wounds dressed with conventional dressings followed by 100 patients who received DACC coated post-operative dressings. Wounds were reviewed at day 5 and day 30 to determine the presence of SSI using the ASEPSIS scoring system. The variation in outcomes between groups was assessed using Chi-Squared test and Logistic regression to assess effects of other variables which may affect healing.

Results: Between 1st August 2015 and 29th February 2016, 120 men and 80 women were recruited. The mean age was 63 (range 27-97) years, 92% were current or ex-smokers and 45.5% were diabetic. Rate of SSI at 5 days was significantly lower in the DACC group compared to standard dressings (1% Vs 10%, $P < 0.05$). There was no difference in the rates of SSI at 30 days. Logistic regression suggested that the type of dressing used was the most prominent predictor variable for the presence of early SSI ($p = 0.028$, OR = 0.09, 95% CI: 0.01, 0.77).

Conclusions: DACC coated dressings were associated with a significant reduction in SSI rates in the early post-operative period.

1. Introduction

Surgical site infections (SSI) are infections occurring at the part of the body where surgery has taken place within 30 days of the procedure, or within one year of the procedure if a prosthetic surgical device was implanted (e.g. mesh, metalwork, vascular graft)¹. SSI account for up to 20% of all hospital acquired infection and occurs in at least 5% of all surgical procedures². Morbidity and mortality due to SSI can be devastating and may be preventable with appropriate strategies and policies in pre, intra and post-operative patient and wound care². One in three post-operative deaths are related at least in part to the presence of a SSI² and mean additional costs incurred in managing a vascular SSI are estimated in the region of £8,500 per patient³.

The incidence of SSI following vascular surgery is 10-15%, rising to 30% in trials specifically monitoring SSI as an outcome^{4,5}. This high incidence is thought to relate to the high rates of co-morbidities, concurrent smoking, diabetes and groin surgery in vascular patients. SSI in vascular surgery are potentially devastating for patients, with 30-40% of SSI in lower limb bypass graft infections resulting in a major amputation⁶ and over one third of all post-operative deaths being attributable, at least in part, to an SSI². Less severe SSI still impact upon patients' wellbeing and quality of life^{7,8}. The hospital costs of SSI are significant with estimates between £1500 and £10,000 per patient episode in vascular surgery^{3,9}[figures updated for 2016 equivalence¹⁰]. Costs are attributable to extended hospital stays, need for re admissions and reoperations, drug treatments, increasingly complex wound management and dressing systems, and high demands on inpatient and community nursing staff. Any strategies to reduce SSI must be investigated for the benefit of patients and also to ensure the best use of limited surgical and healthcare resources.

Post-operative wound dressings act to absorb exudates and protect the wound from the external environment until epithelialisation occurs. A huge range of postoperative dressing options exist, however a 2014 Cochrane review and meta-analysis, which examined data from 20 randomised controlled trials, found no evidence to suggest that any one dressing type was more effective at reducing SSI than any other¹¹.

One newer technology not included in this review was the use of Dialkylcarbamoyl chloride (DACC) as a coating on dressing surfaces. DACC is a highly hydrophobic fatty acid derivative which has recently been incorporated as a coating to the wound contact surface of dressings. Most microorganisms responsible for SSIs have hydrophobic cell surfaces^{12, 13} and when these organisms come into contact with DACC they irreversibly bind via a hydrophobic interaction with the dressing, and are then removed from the wound bed at the next dressing change. This removal of organisms reduces the bioburden at a wound surface¹⁴, thus theoretically preventing the ingress of organisms into the wound and reducing SSI rates.

The aim of this study was to undertake a prospective comparative evaluation of the impact of DACC coated post-operative dressings on the rate of SSI in patients undergoing open non implant vascular surgery, in order to inform the future design of a fully-powered randomised controlled trial.

2. Methods

This was a prospective, non-randomised comparative study in a single vascular surgery centre. A total of 200 participants were recruited, with the initial 100 participants receiving a variety of inert, standard surgical dressings as per the routine clinical practice of the surgeons undertaking the procedure. The second group of 100 participants received DACC coated dressings (Leukomed® Sorbact® – BSN Medical, Hull UK).

2.1 Patients

All adult patients undergoing clean or clean contaminated non-implant vascular surgical procedures were considered for inclusion into the study. Patients undergoing implant-containing vascular surgery were excluded due to the length of time needed for follow-up. Exclusion criteria included known allergy to the DACC dressing components and patients already undergoing treatment with antibiotics. Antibiotic prophylaxis was used as per standard operating procedures.

2.2 Interventions

Procedures were undertaken by or under the supervision of seven vascular consultants and all other aspects of peri-operative care remained unchanged between cohorts. All dressings were applied in a sterile fashion in theatres following wound closure and remained in situ until wound review was undertaken prior to discharge or earlier if required based on clinical need. Standard or DACC coated dressings were continued for the duration of dressing use at that wound site. All patients were discharged home with extra wound dressings to ensure like-for-like dressing changes in the community.

2.3 Outcomes

To assess wound healing we used the ASEPSIS scoring system, which utilises seven clinical parameters to describe satisfactory wound healing (score ≤ 10), impaired wound healing (score 11-20) and SSI (score ≥ 21)¹⁵.

The primary outcome for this study was the presence of SSI (ASEPSIS wound score ≥ 21). Secondary outcomes included evidence of satisfactory healing (ASEPSIS score ≤ 10). Wound assessments were performed on day 5-7 and on day 30. During the assessments, any dressings were removed and a short patient interview and review of patient case notes and prescription chart undertaken to allow comprehensive recording of all wound complications and ASEPSIS score.

2.4 Statistical analysis

Data was collated into *IBM SPSS* (IBM SPSS corporation version 22, Rochester- United States) to facilitate statistical analysis. Data is presented descriptively using mean (sd) or n (%) for each group. The groups were compared using chi-square tests or fishers exact tests for categorical data and t-tests for continuous data (e.g. age). The primary outcome, SSI, was dichotomised into presence or absence of infection and statistical differences between groups were compared using a chi-square tests. In order to measure the association level, crude odds ratio (OR) and the 95% corresponding test-based confidence interval (CI) were calculated. A logistic regression analysis was undertaken to control for the effects of other variables which might be expected to influence healing. A *p*-value of <0.05 was considered statistically significant.

3. Results

200 patients were recruited from 1st August 2015 to 29th February 2016, 120 men and 80 women, with a mean age of 63 (range 27-97) years. Each group had 100 patients. Comparative data for the two groups is summarised in table 1.

Less patients had SSI in the DACC coated group than the standard group at 5-7 days (1/100 and 10/100 respectively, OR = 0.09 (95% CI: 0.01, 0.072, *p*= 0.005). In those remaining at risk, there was no difference in SSI at the 30 day wound assessment (9/99 and 9/90, *p*=0.832). There was no difference in adequate wound healing at any time. ASEPSIS scores recorded for all wounds are summarised in table 2.

For SSI at day 5-7, the single incident of SSI in the DACC dressing group required 7 days of IV antibiotics. In the non-DACC group, all 10 patients with SSI at day 5-7 were treated with antibiotics. 2 of these required IV antibiotics, one for 21 days in total. The other 8 patients were treated with oral antibiotics, with 5/8 treated for 14 days total. At 30 days, there was no significant difference in readmission rates due to SSI between the two groups (7/99 and 9/90, *p*=0.470).

Logistic regression was performed to control for the effects of recorded variables which would be expected to impact upon the risk of SSI as listed in Table 3. Seven potential confounding variables were included in the model¹⁶. After regression analysis, the type of dressing used remained the most prominent predictor in early surgical site infection ($p=0.028$) with an odds ratio of 0.09 (95% CI: 0.01, 0.77).

4. Discussion

This small prospective comparative trial suggests that DACC coating may reduce the rate of SSI in non-implant vascular surgery patients. Prior in-vitro evidence strongly supports the proposed mechanism of action by which DACC might be expected to limit ingress of bacteria into incision wounds^{12, 13, 17}. DACC coated dressings act by trapping and physically removing bacteria, rather than being bactericidal, which in the context of wider societal concerns regarding antibiotic resistance make this action particularly attractive as a novel intervention as the development of bacterial resistance is less likely. They have been shown to bind to organisms that are antibiotic resistant in vitro¹⁷. Results of in-vivo application of DACC coated dressings in chronically infected wounds have also been promising both in terms of bio-burden reduction and enhanced clinical evidence of healing¹⁸⁻²¹. Equally, no absorption of DACC into the wound surface is known to occur and no evidence to date has reported any adverse effects to its use, allowing its potential application to all patient groups.

This study was intended as a pilot to examine the possible effectiveness of DACC impregnated dressings as a prophylactic measure in reducing SSI rate and was able to show a significant reduction in incidence of SSI in a cohort of clean and clean contaminated non-implant vascular surgery with their use. These results are in keeping with recently published evidence supporting the use of DACC coated dressings as prophylaxis against SSI in fit and well patients undergoing caesarean section²². The maximal protective effect appears to be in the early post perioperative period, prior to the 5-7

day assessments. The timing of the apparent action reported in these results appears logical since the mechanism of action of DACC would be prevention of ingress of bacteria into freshly incised wounds which have yet to reepithelialise. Logistic regression suggested a significant impact of the dressings for all instances of SSI when controlling for potential confounding variables expected to impact healing, such as smoking and diabetes.

4.1 Limitations of the study

There were several potential sources of bias within this study. The nature of the study design was as an exploratory proof of concept study prior to an intended randomised trial. Although patients were not randomised, groups were well matched for most variables. There is the possibility that introducing a study, or a study dressing, reduces the rate of measured SSI through observer bias or through bias of the study participant (the so-called Hawthorne effect^{23, 24}). However, although the subjective aspects of the ASEPSIS scoring system were undertaken by a study clinician, treatment for infection, antibiotic use, and infection recorded in the patient case notes were contemporaneous and recorded by the patients' main care team. Patient reported outcomes were not included in the final analysis. Study follow up, at 5-7 days and 30 days, was standardised across both cohorts, so any Hawthorne effect should be seen in both groups.

A further source of bias was the lack of blinding. Leukomed® Sorbact®, the DACC-coated dressing in the study, contains a green colouring to the wound contact layer in order to identify it as a DACC-coated dressing (Shown in Figure 1). Because of this, blinding is difficult, though not impossible to achieve in any trial studying its effects, leading to the open label nature of this study. Future randomised studies into DACC-coated dressings should make use of a wound assessor that is blind to the dressing type used, after removing and disposing of dressings in opaque bags.

5. Conclusion

SSI is a significant problem which is likely to rise as increasing numbers of surgical procedures are performed in an ageing and co-morbid population. Results reported from this study support a growing body of evidence, including a recent systematic review²⁵, that DACC coated hydrophobic dressings have effects in preventing SSI in a number of different patient groups and may have a significant role in future surgical wound management. However, an adequately powered randomised controlled trial comparing DACC coated and conventional dressings is warranted and is now in preparation to provide the robust evidence essential prior to this technology being adopted into routine practice.

Acknowledgements

The authors wish to thank Victoria Allgar, Hull York Medical School, for statistical advice.

References:

1. Horan TC, Gaynes RP, Martone WJ, et al. CDC definitions of nosocomial surgical site infections, 1992: a modification of CDC definitions of surgical wound infections. *Infect Control Hosp Epidemiol.* 1992 Oct;13(10):606-8.
2. National Institute for Health and Clinical Excellence - Surgical Site infections: prevention and treatment. NICE Guideline CG74. 2008 (Updated 2013).
3. Coello R, Charlett A, Wilson J, et al. Adverse impact of surgical site infections in English hospitals. *J Hosp Infect.* 2005 Jun;60(2):93-103.
4. Matatov T, Reddy KN, Doucet LD, et al. Experience with a new negative pressure incision management system in prevention of groin wound infection in vascular surgery patients. *J Vasc Surg.* 2013 Mar;57(3):791-5.
5. Turtiainen J, Saimanen EI, Makinen KT, et al. Effect of triclosan-coated sutures on the incidence of surgical wound infection after lower limb revascularization surgery: a randomized controlled trial. *World J Surg.* 2012 Oct;36(10):2528-34.
6. Siracuse JJ, Nandivada P, Giles KA, et al. Prosthetic graft infections involving the femoral artery. *J Vasc Surg.* 2013 Mar;57(3):700-5.
7. Bayat A, McGrouther DA, Ferguson MW. Skin scarring. *BMJ.* 2003 Jan 11;326(7380):88-92.
8. Astagneau P, Rioux C, Golliot F, et al. Morbidity and mortality associated with surgical site infections: results from the 1997-1999 INCISO surveillance. *J Hosp Infect.* 2001 Aug;48(4):267-74.
9. Tanner J, Khan D, Aplin C, et al. Post-discharge surveillance to identify colorectal surgical site infection rates and related costs. *J Hosp Infect.* 2009 Jul;72(3):243-50.
10. Curtis L BA. The Hospital & community health services (HCHS) index. Unit costs of health and social care - Personal and Social Services Research Unit UK. 2015 (Section 16.3):242.
11. Dumville JC, Gray TA, Walter CJ, et al. Dressings for the prevention of surgical site infection. *Cochrane Database Syst Rev.* 2014 (9):CD003091.
12. Cowan MM, van der Mei HC, Rouxhet PG, et al. Physico-chemical and structural properties of the surfaces of *Peptostreptococcus micros* and *Streptococcus mitis* as compared to those of mutants streptococci, *Streptococcus sanguis* and *Streptococcus salivarius*. *J Gen Microbiol.* 1992 Dec;138(12):2707-14.
13. Ljungh A, Hjerten S, Wadstrom T. High surface hydrophobicity of autoaggregating *Staphylococcus aureus* strains isolated from human infections studied with the salt aggregation test. *Infect Immun.* 1985 Feb;47(2):522-6.
14. Ljungh A, Yanagisawa N, Wadström T. Using the principle of hydrophobic interaction to bind and remove wound bacteria. *Journal of Wound Care.* 2006;15:175-80.
15. Wilson AP, Treasure T, Sturridge MF, et al. A scoring method (ASEPSIS) for postoperative wound infections for use in clinical trials of antibiotic prophylaxis. *Lancet.* 1986 Feb 8;1(8476):311-3.
16. Vittinghoff E, McCulloch CE. Relaxing the rule of ten events per variable in logistic and Cox regression. *American journal of epidemiology.* 2007 Mar 15;165(6):710-8.
17. Ronner AC, Curtin J, Karami N, et al. Adhesion of methicillin-resistant *Staphylococcus aureus* to DACC-coated dressings. *J Wound Care.* 2014 Oct;23(10):484, 6-8.
18. Bullough L, Little G, Hodson J, et al. The use of DACC-coated dressing for the treatment of infected complex abdominal wounds; a case report *Wounds UK.* 2012;8(4):102-9.
19. Gentili V, Gianesini S, Balboni PG, et al. Panbacterial real-time PCR to evaluate bacterial burden in chronic wounds treated with Cutimed Sorbact. *Eur J Clin Microbiol Infect Dis.* 2012 Jul;31(7):1523-9.
20. Kleintjes WG, Schoeman D, Collier L. A pilot study of Cutimed® Sorbact® versus ACTICOAT™ versus Silverlon® for the treatment of burn wounds in a South African adult burn unit. *Wound healing South Africa.* 2015;8(2):22-9.
21. Mosti G, Magliaro A, Mattaliano V, et al. Comparative study of two antimicrobial dressings in infected leg ulcers: a pilot study. *J Wound Care.* 2015 Mar;24(3):121-2; 4-7.

22. Stanirowski PJ, Bizon M, Cendrowski K, et al. Randomized Controlled Trial Evaluating Dialkylcarbamoyl Chloride Impregnated Dressings for the Prevention of Surgical Site Infections in Adult Women Undergoing Cesarean Section. *Surg Infect (Larchmt)*. 2016 Feb 18.
23. Roethlisberger FJ, Dickson WJ, Wright HA, et al. *Management and the worker : an account of a research program conducted by the Western Electric Company, Hawthorne Works, Chicago*. Cambridge, Mass.: Harvard University Press; 1939.
24. McCarney R, Warner J, Iliffe S, et al. The Hawthorne Effect: a randomised, controlled trial. *BMC medical research methodology*. 2007;7(1):1.
25. Totty JP, Bua N, Smith GE, et al. Dialkylcarbamoyl chloride (DACC)-coated dressings in the management and prevention of wound infection: a systematic review. *Journal of Wound Care*. 2017 Mar;26(3):107-14.

Legends for tables and figures

Table 1: Participants demographics, ASA grades and surgical procedure undertaken in standard and DACC coated dressing groups. Two tailed P values reported from Student t tests and Chi-square test with Yates correction, ** signifies a significant difference between patient groups.

Table 2: Results of ASEPSIS scores at assessments throughout study. Two tailed P values reported from Chi-square test with Yates correction, ** signifies significant difference between patient groups.

Table 3. Potential confounders to SSI included in Logistic regression. Type of surgery is divided into treatment for critical limb ischaemia vs other vascular surgery (** = $p < 0.05$, df = degrees of freedom, Sig.= significance, OR = odds ratio, CI = confidence interval, BMI = Body mass index, SSI = Surgical site infection, ASA = American Society of Anaesthesiologists)

Figure 1: Photographs of Leukomed® Sorbact®, the DACC-coated dressing used in the trial, against a white background. The coloured nature of the wound contact layer is demonstrated.