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Effects of the application of vitamin E and silicone dressings vs conventional dressings on incisional surgical site infection in elective laparoscopic colorectal surgery: a prospective randomized clinical trial

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SUMMARY

Aim: To compare the effect of conventional wound dressings (CD) with vitamin E and silicone (E-Sil) dressings on incisional surgical site infection (SSI) in patients undergoing elective colorectal laparoscopic surgery.

Patients and methods: A prospective, randomized study was performed. Patients were assigned at random into two groups: an E-Sil group and a CD group. Incisional SSI, postoperative pain and acute phase reactants were investigated.

Results: In total, 120 patients were included in this study (60 in each group). The incisional SSI rate was 3.4% in the E-Sil group and 17.2% in the CD group ($P = 0.013$). *Bacteroides fragilis* alone grew in the cultures of infected wounds in the E-Sil group, while cultures for infected wounds in the CD group were polymicrobial. Mean postoperative pain 48 h after surgery was 27.1 [standard deviation (SD) 10.7] mm in the E-Sil group and 41.6 (SD 16.9) mm in the CD group ($P < 0.001$). White blood cell (WBC) count and C-reactive protein (CRP) level were lower in the E-Sil group, even after the exclusion of patients presenting with postoperative complications.

Conclusion: Use of an E-sil dressing to cover the Pfannestiel wound after elective laparoscopic colorectal surgery leads to a reduction in the incisional SSI rate, lower postoperative pain, and a decrease in CRP level and WBC count.

Introduction

Surgical site infection (SSI) is a frequent complication after surgery, resulting in decreased health-related quality of life, increased risk of re-admission and prolonged hospital stay, leading to increased hospital costs [1,2]. Elective colorectal surgery is associated with incisional SSI rates between 5% and 15% [1]. Although the laparoscopic approach has reduced the incidence of incisional SSI significantly, this complication remains a challenge for colorectal surgeons.

Several interventions have been adopted to reduce the incidence of incisional SSI, including peri-operative antibiotic

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systemic prophylaxis, skin cleansing with antiseptic agents, adequate surgical technique, thermoregulation and glycaemic control [3,4].

The influence of postoperative wound care and the use of different types of dressings has been widely studied [3,5]. The use of total occlusive ionic silver-containing dressings was found to be effective in reducing bacterial colonization on the surgical site compared with no dressing [6]. A recent study by the authors' group demonstrated that topical application of mupirocin ointment achieves better results for the prevention of SSI than ionic silver-containing dressings or standard dressings in patients undergoing elective open colorectal surgery [7].

The aim of this study was to compare the effect of conventional wound dressings (CD) with vitamin E and silicone (E-Sil) dressings on incisional SSI in patients with colorectal cancer undergoing elective laparoscopic surgery.

Methods

A prospective, randomized study was performed at the study institution between January and December 2017. Inclusion criteria were a diagnosis of colorectal neoplasms and plans to undergo an elective laparoscopic procedure with curative aims. Exclusion criteria were open surgical approach or conversion to laparotomy, performance of a stoma, immunodepressive status (human immunodeficiency virus or congenital immunodeficiencies, and pharmacologically induced immunodeficiencies by chemotherapeutic agents or corticoids) and anastomotic leak in the postoperative course, confirmed by computed tomography scan with rectal contrast enema. Patients with rectal cancer receiving neoadjuvant treatment were also excluded.

The sample size calculation was based on historic data for the study centre's incisional SSI rate in elective colorectal surgery (18%) and an expected incisional SSI rate of 6% in the experimental group (E-Sil group). At 80% power and a significance level of 0.05, it was calculated that 57 patients were required in each arm of the study. The number of patients was increased by 5% in anticipation of postoperative anastomotic leaks; therefore, 60 patients were included in each group.

Patients were assigned at random in a 1:1 allocation scheme using a random number table into two groups: an E-Sil group and a CD group (Figure 1).

This study was approved by the local ethics committee. Informed consent was obtained from all participants.

Surgical methods

Peri-operative systemic antibiotics (cefuroxime 1500 mg and metronidazole 1500 mg; single dose pre-operatively, within 30 min of incision and re-dosed when the surgery exceeded 4 h or intra-operative blood loss exceeded 1500 mL) were used in both groups. No mechanical bowel preparation took place in any patient.

An aqueous solution of 10% povidone-iodine was applied to the skin pre-operatively. The resected tissue was extracted through a 6-cm suprapubic Pfannenstiel incision, enlarging the port placed at this level. The incision was protected with an Alexis device (Applied Medical, Rancho Santa Margarita, CA, USA) to avoid contact between the resected tissue and the abdominal wall. The aponeurotical layer was sutured with polydioxanone loop number 1 (Ethicon, Johnson & Johnson, Somerville, NJ, USA). The fascial layer of the other port sites was not closed. The skin was closed with staples. After placing the staples, povidone-iodine solution was re-applied to the wound. Once the skin had dried, an E-Sil dressing (VEA Sil, Hulka SRL, Italy) was placed over the Pfannenstiel incision in the E-Sil group, and covered with gauze and plastic adhesive tape. This primary dressing was covered with a CD. In the CD group, the Pfannestiel wound was covered with gauze and plastic adhesive tape. This dressing was covered by a second CD. The second dressing was the same for both groups in order to blind the patients, the nursing and medical staff, and the independent data collector (epidemiology nurse) regarding the type of dressing. The other ports were covered with CDs.

Dressings were removed on postoperative day 5, as per protocol, or earlier if SSI was suspected. SSI was suspected when a patient presented with fever; a red, painful and tender region adjacent to the dressing; or the dressing was impregnated with a liquid suspicious of purulent discharge.

Variables

Clinical variables investigated were age, sex, comorbidities, location of the neoplasm, complications (anastomotic leak, incisional and organ/space SSI), mortality and hospital stay. Surgical technique was recorded. Microbiological variables included cultures of the patients with incisional SSI. Postoperative pain was evaluated 24 h after surgery using a visual analogue scale (VAS), ranging from 0 mm (complete absence of pain) to 100 mm (unbearable pain). Acute phase reactants [white blood cell (WBC) count, fibrinogen, C-reactive protein (CRP) and lactate] were measured 48 h after surgery.

Incisional SSI was defined following the criteria of the US Centers for Disease Control and Prevention [8]. When a purulent discharge from the surgical incision was present, a sample was obtained for microbiological confirmation. Incisional SSI was determined by an epidemiology nurse blinded to the treatment groups. Infection surveillance was extended for 30 days after discharge; all patients were evaluated 30 days after surgery in the outpatient clinic. If the patients presented with symptoms suggestive of SSI before the 30-day visit, they were advised to go to the emergency department. Once incisional SSI was diagnosed, the incision was opened and the purulent discharge was drained.

Statistics

Statistical analysis was performed using SPSS 22.0 for Windows (IBM Corp., Armonk, NY, USA). Quantitative variables that followed a normal distribution were defined by the mean and standard deviation (SD). For non-Gaussian variables, the median and range were used. Qualitative variables were defined by number and percentage of cases.

Comparison of variables was performed using Student's *t*-test and the Pearson correlation method for quantitative variables following a Gaussian distribution. Non-parametric tests (Mann–Whitney and Spearman correlation) were used for non- Gaussian variables. Comparison of qualitative variables was performed using Chi-squared test; in those cases with fewer than five observations in the cell, Fisher's exact probability method was used ($P < 0.05$ was regarded as significant).

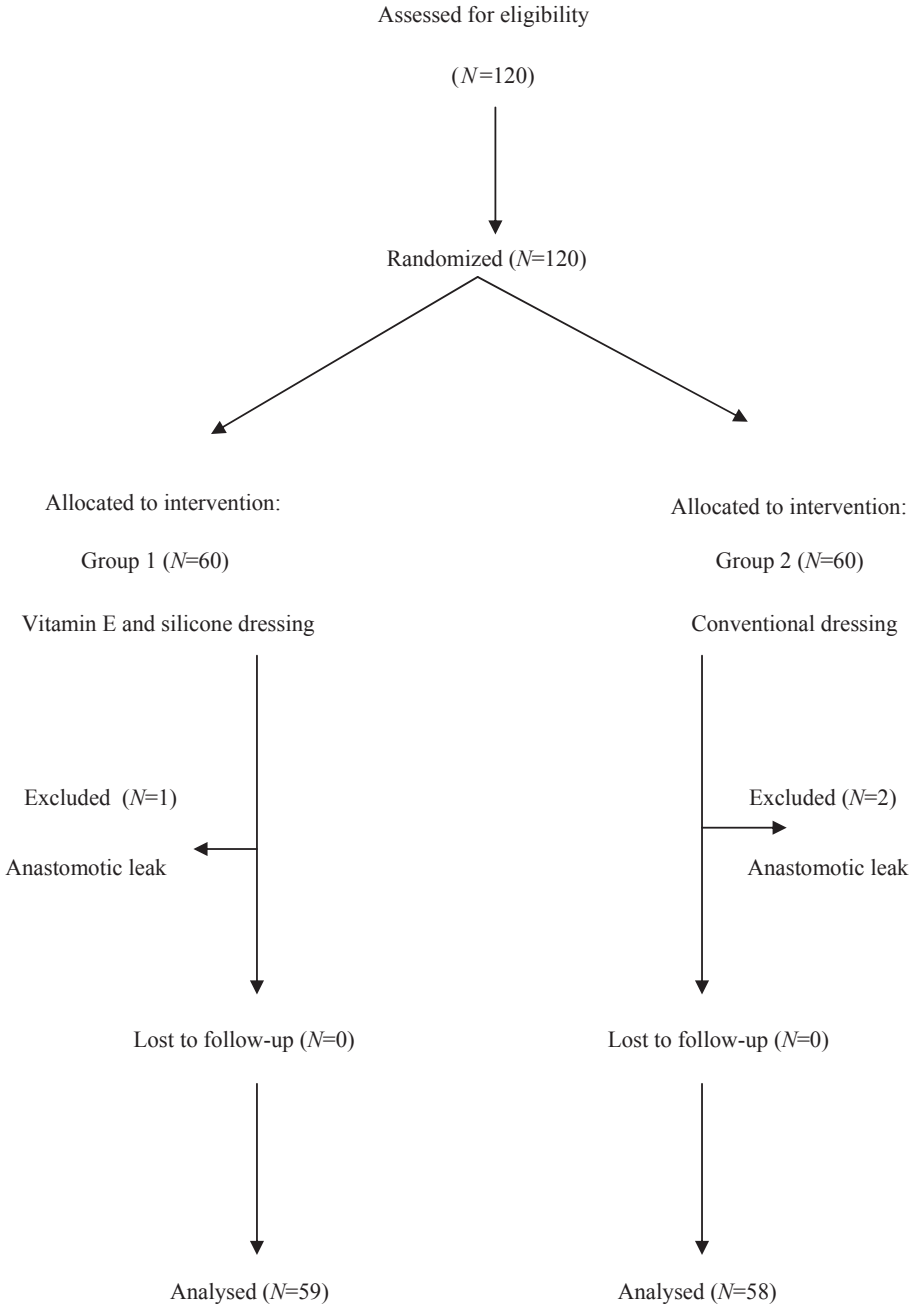

Figure 1. CONSORT flow diagram.

Results

In total, 120 patients were assessed for eligibility. Three patients were excluded from the analysis as they presented with an anastomotic leak. In total, 59 and 58 patients were analysed in the E-Sil and CD groups, respectively. The patient sample consisted of 72 males (61.5%) and 45 females (38.5%), with a mean age of 67.2 (SD 10.4) years. Patient comorbidities for both groups are described in Table I.

The tumours were located in the right colon ($N = 45$, 37.5%), the transverse colon ($N = 3$, 2.5%), the left colon ($N = 60$, 50%) and the rectum ($N = 12$, 10%). The surgical techniques are described in Table II. There were no significant differences in surgical techniques between the groups. All the anastomoses were stapled: a circular stapler (EEA 28 mm, Medtronic,

Table I
Distribution of comorbidities between groups

	Vitamin E and silicone dressing group	Conventional dressing group	*P*-value
N	59	58	
Type 2 diabetes mellitus	15 (25.4%)	14 (24.1%)	NS
Hypertension	24 (40.7%)	26 (44.8%)	NS
Dyslipidaemia	16 (27.1%)	14 (24.1%)	NS
Cardiopathy	9 (15.2%)	7 (12.1%)	NS
Chronic obstructive pulmonary disease	3 (5.1%)	3 (5.2%)	NS

NS, not significant.

Table II
Distribution of surgical procedures performed between groups

Surgical procedure	Vitamin E and silicone dressing group	Conventional dressing group	*P*-value
Left colectomy	5	5	NS
Sigmoidectomy	24	26	NS
Right colectomy	25	23	NS
Upper anterior resection of rectum	6	6	NS

NS, not significant.

Minneapolis, MN, USA) was used in the left colon and the rectum, and a lineal stapler was used in ileocolic anastomoses. Ileocolic anastomoses were performed extracorporeally through the Pfannenstiel incision. Colorectal anastomoses were performed intracorporeally. The specimen was extracted through the Pfannenstiel incision in all cases.

Anastomotic leaks occurred in three patients (2.5%), including one patient in the E-Sil group and two patients in the CD group [non-significant (NS)]. All the anastomotic leaks occurred in colorectal anastomoses. Organ/space SSI occurred in three patients in each group (NS). There were no deaths in either group. Median hospital stay was five days (range four to 26 days) in the E-Sil group and seven days (range five to 35 days) in the CD group ($P < 0.001$).

Incisional SSI in the Pfannestiel incision occurred in two (3.4%) patients in the E-Sil group and 10 (17.2%) patients in the CD group [odds ratio (OR) 6.1, 95% confidence interval (CI) 1.27–21.3; $P = 0.013$]. In all cases, incisional SSI presented as redness around the incision; the wound was opened and purulent discharge drained. The results of cultures of the wound discharge are described in Table III. These micro-organisms were not resistant to the peri-operative systemic antibiotics administrated. There was no significant association between any of the comorbidities and incisional SSI. The type of operation did not show any impact on SSI. The other ports did not develop incisional SSI.

Mean postoperative pain, as quantified by VAS 48 h after surgery, was 27.1 (SD 10.7) mm in the E-Sil group and 41.6 (SD 16.9) mm in the CD group (mean difference 20.5 mm, 95% CI 8.4–42.1; $P<0.001$).

Effect on acute phase reactants 48 h after surgery

Mean values of evaluated acute phase reactants are shown in Table IV. WBC count was significantly lower in the E-Sil group (mean difference 2202/m^3, 95% CI 981.9–3617.5; $P = 0.003$).

Table III
Wound culture results in the two groups

	Vitamin E and silicone dressing group	Conventional dressing group
Escherichia coli	0	9 (90%)
Streptococcus spp.	0	4 (40%)
Klebsiella spp.	0	2 (20%)
Bacteroides fragilis	2 (100%)	2 (20%)

Table IV
Distribution of acute phase reactant levels between groups

Acute phase reactants	Vitamin E and silicone dressing group	Conventional dressing group	*P*-value
WBC count (WBC/mm^3)	8412 (1817)	10,614 (2866)	0.003
Fibrinogen (mg/dL)	587.6 (91.6)	599.2 (101.2)	0.389
C-reactive protein (mg/dL)	8.7 (6.6)	11.9 (6.1)	0.016
Lactate (mg/dL)	1.1 (1)	1.3 (1.1)	0.328
Exclusion of patients with complications			
N	54	45	
WBC count (WBC/mm^3)	7605 (1517)	9708 (2696)	0.001
Fibrinogen (mg/dL)	507.5 (85.6)	529.3 (118.2)	0.282
C-reactive protein (mg/dL)	6.7 (3.4)	9.2 (4)	0.022
Lactate (mg/dL)	0.9 (0.8)	1 (0.8)	0.448

WBC, white blood cells.
Values are mean (standard deviation).

CRP level was also lower in the E-Sil group (mean difference 3.2 mg/dL, 95% CI 0.9–11.5; $P = 0.016$). There were no significant differences in fibrinogen and lactate values between the two groups.

After exclusion of the patients with postoperative complications in both groups, the WBC count 48 h after surgery was significantly lower in the E-Sil group (mean difference 2103/mm^3, 95% CI 773–4354; $P = 0.001$). CRP level was also lower in the E-Sil group (mean difference 2.5 mg/dL, 95% CI 1.1–9.6; $P = 0.022$).

Discussion

It has been widely demonstrated that vitamin E has an immunomodulative effect, affecting humoral and cell-mediated immune responses. Vitamin E modulates neutrophil recruitment to damaged tissue [9]. Topical application of vitamin E ointment has demonstrated a certain anti-inflammatory effect in dermatological diseases. Vitamin E reduces oedema and moderates the increase of cyclo-oxygenase-2, an enzyme that catalyses the synthesis of prostaglandin E2, involved in the local inflammatory response to stimuli [10]. It has also been widely used in gynaecological disorders, mainly affecting the vulvar skin and vaginal mucosae [11]. Postoperatively, vitamin E is used for cosmetic effect, as reduction of the local inflammatory response is associated with a smaller scar. Moreover, it has been demonstrated that vitamin E is associated with a reduction in postoperative pain from skin wounds and after haemorrhoidectomy [12,13].

This study used a dressing combining a thin silicone lamina with vitamin E. Silicone patches over wounds have been shown to prevent hypertrophic scars, as silicone induces correct hydration of the skin, reduces the inflammatory mediators and modulates the synthesis of collagen. Together, these factors reduce wound tension and improve healing [14]. The combination of vitamin E and silicone has a synergistic effect on immunomodulation and wound healing.

It is widely known that different inflammatory responses to the local stimulus can contribute to the development of SSI [3]. A recent study by the authors' group showed that the application of vitamin E ointment to subcutaneous tissue in elective laparoscopic colorectal surgery reduced the incidence of incisional SSI, postoperative pain, hospital stay and analytical acute phase reactants [15]. The results obtained in the present study are very similar, despite the fact that vitamin E was included in the dressing rather than applied to the wound directly.

The only micro-organisms causing incisional SSI in the E-Sil group were *Bacteroides fragilis*; this finding is similar to the results obtained previously with subcutaneous application of vitamin E [15]. This may suggest that the vitamin E included in the dressing has an immunomodulatory effect beyond the surface of the skin. Vitamin E acts as cofactor in the hydrogenization of unsaturated fatty acids, induced by anaerobic micro-organisms alone, leading to local reduction of these fatty acids, including omega-3 fatty acids, in the subcutaneous tissue. Omega-3 fatty acids have demonstrated a bacteriostatic and bactericidal effect [16,17]. This may explain the resistance of anaerobic bacteria to the bactericidal and immunomodulatory effect of vitamin E.

Acute phase reactants are produced during infection, but are also produced in response to inflammation which is part of the normal postoperative course after surgery. However, it has been shown that the elevation of acute phase reactants is significantly higher in patients developing complications than in patients with an uneventful postoperative course [18]. This study found that the WBC count and CRP level were significantly higher in the CD group; however, as the incisional SSI rate was greater in these patients, the higher WBC count and CRP level could be attributed to an incipient infection. As such, an analysis was performed, excluding the patients presenting with complications from both groups; this showed that the WBC count and CRP level remained lower in the E-Sil group than the CD group. This reflects that, beyond a protective effect against incisional SSI, use of E-Sil dressings induces an immunomodulatory effect, reducing the release of pro-inflammatory mediators from surgery. The clinical translation of this lower inflammatory response induced by vitamin E is lower pain perception, as measured by VAS 48 h after surgery.

In conclusion, use of an E-Sil dressing to cover the Pfannestiel wound after elective laparoscopic colorectal surgery leads to a reduction in the incisional SSI rate, lower postoperative pain, and decreased CRP level and WBC count 48 h after surgery compared with the use of a CD.

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Conflicts of interest statement
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