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Original Article

Does Wound Irrigation with Clorhexidine Gluconate Reduce the Surgical Site Infection Rate in Closure of Temporary Loop Ileostomy? A Prospective Clinical Study

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Abstract

Background: The aim of this study was to investigate the effect of irrigating the surgical site with 0.05% chlorhexidine gluconate (CHG) on surgical site infection (SSI) in temporary loop ileostomy closure.
Methods: In this observational cohort, patients who underwent diverting loop ileostomy and elective ileostomy closure for any reason between September 2014 and July 2016 were enrolled. Irrigation of the surgical site with 0.05% CHG or saline were compared regarding post-operative incision complications. Infection risk was estimated by the National Nosocomial Infection Surveillance System (NNIS) and Study of the Effect of Nosocomial Infection Control (SENIC) scores. Post-operative follow-up was performed by a surgeon blinded to the treatment. Diagnosis of SSI was recorded according to the Guidelines for Prevention of Surgical Site Infection. Wound healing was evaluated by the Additional treatment, Serous discharge, Erythema, Purulent exudate, Separation of the deep tissues, Isolation of bacteria, and the duration of inpatient Stay (ASEPSIS) score.
Results: There were 122 patients meeting the inclusion criteria: 60 in the saline (control) and 62 in the CHG (study) group. The mean age was 56.5 ± 13.5 (standard deviation [SD]); 74 patients were male. The groups were similar regarding age, sex, indication for ileostomy, neoadjuvant therapies, and SENIC and ASEPSIS scores. The overall SSI rate was 18%: 19 patients (31.6%) in the control group and 3 (4.8%) patients in the study group ($p < 0.001$). The mean ASEPSIS score was higher in the control group (12.8 ± 17.7) than in the study group (3.7 ± 7.8) ($p < 0.001$). Patients in the control group had significantly higher rates of seroma (13.3% vs 1.6%; $p = 0.014$) and incision dehiscence (31.6% and 4.8%; $p = 0.001$). Time to healing was 9.9 ± 5.1 days in the control group and 7.3 ± 5.3 days in the study group ($p = 0.007$).
Conclusions: Irrigation of the incision with 0.05% CHG reduces the SSI rate compared with saline irrigation. There is a need for randomized and wider trials to clarify the effect and standards of incision irrigation.

Keywords: chlorhexidine gluconate; ileostomy closure; incision irrigation

Temporary loop ileostomy is used frequently in the treatment of many colorectal diseases, including rectal cancer, inflammatory bowel disease, intestinal perforation, and fistulas. Patients with temporary loop ileostomy after total mesorectal excision for rectal cancer have significantly lower morbidity and re-operation requirements secondary to anastomotic leak than do those without ileostomy [1–3]. However, complications such as surgical site infection (SSI), small-bowel obstruction, and anastomotic leak remain major problems. The most common complication after ileostomy closure is SSI, with a reported incidence between 2%–34% [4–7].

Chlorhexidine gluconate (CHG) is a topical antiseptic in widespread clinical use. Its safety and efficiency have been known for more than 50 years [8–10]. It has a broad spectrum covering gram-negative, gram-positive, and non-spore-forming bacteria as well as yeast and human immunodeficiency virus

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[11–13]. A 0.5% solution prepared with distilled water has been reported to provide more effective pre-operative skin antisepsis and intra-operative antiseptic effect with irrigation of incisions and prosthetic material than many other agents [14]. This study investigated the effects of irrigating the surgical site with 0.05% CHG on SSI and incision healing after ileostomy closure.

Patients and Methods

The Dokuz Eylul University Ethics Committee (No:Deu-NA13647) approved the study. Informed consent for the surgical procedure and also for collecting and using data in clinical studies was received from all patients. This was an observational cohort study. The prospectively recorded database of the patients who underwent intestinal surgery was reviewed retrospectively. In our institution, one of the surgeons (CT) has been irrigating the surgical site routinely with 0.05% CHG after ileostomy closure since September 2014, whereas the other surgeons (TE, AEC) have been performing routine saline irrigation. Patients who underwent diverting loop ileostomy and elective ileostomy closure for any reason between September 2014 and July 2016 were tiered into two groups. The results of 0.05% CHG (study group) and saline irrigation (control group) were compared. The management of the patients was similar between groups except for the irrigation solution.

Exclusion criteria were active infection or use of antibiotics within four weeks before surgery, immunosuppression, presence of para-stomal hernia, liver or kidney dysfunction, short bowel syndrome, history of hypersensitivity to cefuroxime axetil or metronidazole, additional procedures other than ileostomy closure, and post-operative antibiotic treatment for any reason (pneumonia, urinary tract infection, etc.). Ileostomy closures with small-bowel resection and side-to-side stapled anastomoses were analyzed for the study. Any other surgical procedure (without small bowel resection, hand-sewn anastomosis) was excluded. A flow diagram of the study is given in Figure 1.

Infection risk was evaluated by the National Nosocomial Infection Surveillance System (NNIS) [15] and Study of the Effect of Nosocomial Infection Control (SENIC) [16], which were recorded for all patients. These scoring systems represent the risk of post-operative infections according to surgical procedure, incision classification, patient performance, comorbidities, and operative time.

Surgical technique

Our routine time for closure of ileostomy is three months. We do not attempt surgery before this time because of potential hostile adhesions. Some of the patients have the operation even later if the adjuvant chemotherapy has not been stopped temporarily.

Mechanical bowel preparation was not performed before ileostomy closure. All the patients were operated on under general anesthesia, and a single dose of cefazolin was administered intravenously 30 minutes before the skin incision. In accordance with our guidelines for anti-microbial prophylaxis of our local infection control committe, we use only cefazolin before small-intestinal surgery and cefazolin plus metronidazole before large-bowel surgery. The surgical site was shaved, and skin antisepsis was achieved using 10% povidone– iodine

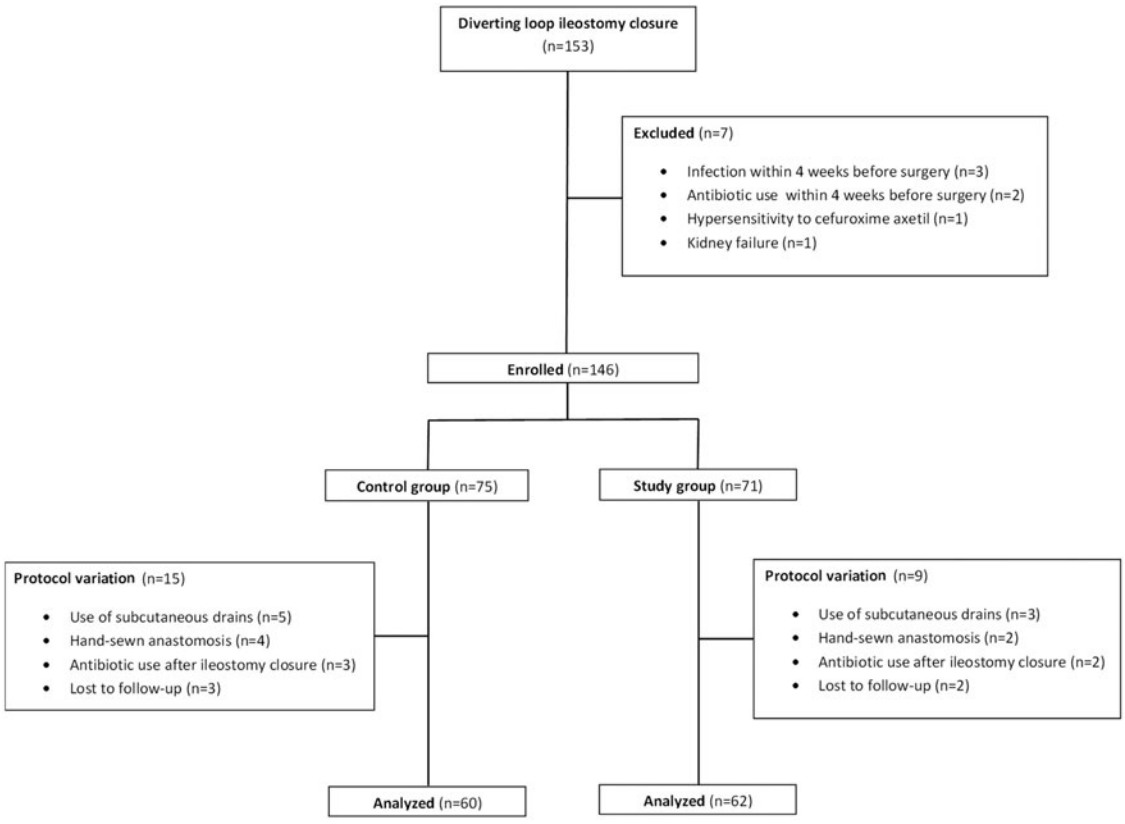

FIG. 1. Flow chart of study.

solution. The skin edges of the stoma were incised, and the small bowel was dissected from the abdominal wall and mobilized to outside the abdomen. A short segment of the small bowel including the stomal region was resected. A side-to-side anastomosis was performed with linear stapler (GIA® 80-3.8 mm and TA® 45-3.5 mm; Medtronic, Minneapolis, MN USA). The fascia was closed with 2-0 polydioxanone (PDS® II 36 mm; Ethicon, Somerville, NJ USA).

The surgical site was irrigated after closure of the fascia for 1 minute with 1 liter of 0.05% CHG in distilled water (Acar Kimya, Istanbul, Turkey) in the study group and 0.09% saline in the control group. The skin was closed with the stapler.

Post-operative follow-up and definition of surgical site infection

Incision care and post-operative follow-up was performed by a surgeon (MG) blinded to the study groups and recorded on post-operative days 1, 2, 3, 5, 7, 15, and 30. Dressings were changed on post-operative days 1 and 2 and removed on post-operative day 3. Samples were obtained for microbiologic culture in case of discharge from the incision. Purulent drainage from the incision or positive culture was considered an SSI. Inflammation, localized swelling, tenderness, pain, and redness around the surgical site were assessed. High fever accompanied by at least one of these signs also was recorded as SSI. Classification of SSI was recorded according to the 1999 Guidelines for Prevention of Surgical Site Infection [17]. Infections occurring within 30 days and involving only the skin or subcutaneous tissue were recorded as superficial SSI and those involving deeper soft tissues (fascia and muscle layers) as deep SSI. Incision healing was evaluated by the ASEPSIS score on post-operative days 1, 2, 3, 5, and 7 [18]. Complete healing was defined as removal of the skin stapes in patients without complications and skin closure after negative culture in patients with incision complications.

Sample size and statistical analysis

An SSI rate of 30% was predicted when calculating the sample size. With the hypothesis that irrigation with 0.05% CHG would reduce the SSI ratio to 4%, the sample size was calculated as 60 patients in each group with $\alpha = 0.05$ and 95% power.

Continuous variables were expressed as means and range and categorical variables as frequency and percentages. Association between categorical variables and morbidity was determined with the χ^2 test. Association between continuous variables and morbidity was tested by the independent samples *t* test. $P < 0.05$ was defined as statistically significant.

Results

Of the 153 patients, 122 were included in the study: 60 in the control group, and 62 in the study group (Fig. 1). The mean age was 56.5 ± 13.5 years. Seventy-four patients (60.7%) were male. The groups were similar regarding age, sex, indication for ileostomy, neoadjuvant treatments, pre-operative albumin concentration, smoking history, time from creation to closure of the ileostomy, and operative time. Mean ASEPSIS and SENIC scores were not significantly different in the two groups. Patients in the study group had a significantly higher Body Mass Index (BMI) (26.7 ± 3.6) than those in the control group (24.6 ± 2.9) ($p = 0.001$). Details of demographic and operative characteristics are given in Table 1.

The overall SSI rate was 18% (n = 22). Nineteen patients (31.6%) in the control group and 3 patients (4.8%) in the study group had SSI ($p < 0.001$). Those patients all had partial or complete incision dehiscence. Seroma without infection was seen in eight patients (13.3%) in the control group, significantly fewer than in the study group (n = 1; 1.6%; $p = 0.014$). In the study group, the time to healing was shorter (7.3 ± 5.3 days) than in the control group (9.9 ± 5.1 days; $p = 0.007$). The mean hospital stay was 11.3 ± 5.3 days in the control group, longer than in the study group (9.3 ± 6.5), but the difference was not

Table 1. Demographic and Surgical Characteristics

	Control group (n = 60)	*Study group (n = 62)*	p
Mean age (±SD) (y)	55.5 ± 12.1	57.5 ± 14.1	0.388[a]
Gender (%)			0.142[b]
Female	27 (45)	21 (33.9)	
Male	33 (55)	41 (66.1)	
BMI (±SD) (kg/m^2)	24.6 ± 2.9	26.7 ± 3.6	**0.001**[a]
Indication for ileostomy (%)			
Rectal cancer	38 (64)	38 (61)	0.816[b]
Other	22 (36)	24 (39)	
Neoadjuvant chemoradiotherapy (%)	31 (51.6)	38 (61.3)	0.187[b]
Pre-operative albumin concentration (±SD) (g/dL)	3.9 ± 0.4	3.9 ± 0.3	0.718
Smoking (%)	26 (43.3)	29 (46.8)	0.421[a]
Mean ASEPSIS score (±SD)	2.13 ± 0.34	2.21 ± 0.45	0.294
Mean SENIC score (±SD)	1.12 ± 0.32	1.13 ± 0.53	0.112
Mean duration with ileostomy (±SD) (mos)	9 ± 6	9.4 ± 8.4	0.800[a]
Mean operative time (±SD) (min)	74.67 ± 11.7	75 ± 12.3	0,700[a]

Statistically significant values are in **boldface** type.
[a] *t*-test.
[b] χ^2 test.
ASEPSIS = Additional treatment, Serous discharge, Erythema, Purulent exudate, Separation of the deep tissues, Isolation of bacteria, and the duration of inpatient Stay; BMI = Body Mass Index; SD = standard deviation. SENIC = Study of the Effect of Nosocomial Infection Control.

Table 2. Post-Operative Results and Details of Complications

	Control group (n = 60)	*Study group* (n = 62)	p
Seroma (%)	8 (13.3)	1 (1.6)	**0.014**[a]
Incision dehiscence (%)	19 (31.6)	3 (4.8)	**0.001**[b]
Partial	8 (13.3)	2 (3.2)	
Complete	11 (18.3)	1 (1.6)	
Surgical site infection (%)	19 (31.6)	3 (4.8)	**<0.001**[b]
Superficial	13 (21.6)	2 (3.2)	
Deep	6 (10)	1 (1.6)	
Mean time to healing (±SD) (d)	9.9 ± 5.1	7.3 ± 5.3	**0.007**[a]
Mean hospital stay (±SD (d)	11.3 ± 5.3	9.3 ± 6.5	0.064[a]
Mean ASEPSIS score (±SD)	12.8 ± 17.7	3.7 ± 7.8	**<0.001**[a]

Statistically significant values are in **boldface** type.
[a] *t*-test.
[b] χ^2 test.
ASEPSIS = Additional treatment, Serous discharge, Erythema, Purulent exudate, Separation of the deep tissues, Isolation of bacteria, and the duration of inpatient Stay; SD = standard deviation.

statistically significant. The mean ASEPSIS score was significantly lower in the study group (3.7 ± 7.8 vs. 12.8 ± 17.7; $p < 0.001$) (Table 2).

Discussion

Loop ileostomy is a frequently performed procedure to prevent anastomotic complications or provide fecal diversion. In parallel with higher numbers of distal rectal surgery procedures and neoadjuvant radiotherapy in recent years, the use of loop ileostomy has been increasing gradually. However, post-operative complications related to ileostomy closure remain as a serious problem. Incisional complications are the major cause of morbidity [19, 20]. In our study, the incidence of SSI in both groups was 18%, which is consistent with reports in the literature.

Many factors, including age, sex, BMI, surgical technique, operative time, co-morbidities, time from creation to closure of the ileostomy, and neoadjuvant and adjuvant treatments have been suggested to be associated with morbidity after ileostomy closure [21–24]. Our groups were similar in terms of demographic and surgical characteristics except for BMI. Patients in the study group had higher mean BMIs, which might be associated with a higher incidence of SSI. We think that this difference was not linked to a selection bias. The estimated SSI risk was assessed with ASEPSIS and SENIC scores, which were not different in the two groups.

Several studies have investigated the impact of skin closure and anastomotic techniques, use of subcutaneous drains, and timing of closure to prevent post-operative complications after ileostomy closure [25–28]. Circumferential purse-string suturing has been suggested to reduce the SSI rate from 30% to 8% compared with primary closure in a randomized controlled trial [26]. However, there are studies reporting no significant difference between purse-string and primary sutures [29,30]. A recent meta-analysis including 2,921 cases concluded that purse-string suturing was the most favorable among six techniques (primary closure, primary closure with drain, loose primary closure, secondary closure, delayed primary closure) with the lowest SSI risk (odds ration [OR] 0.12). In our institution, we prefer stapler anastomosis and primary closure with skin staples; thus, we could not assess this issue.

The duration between ileostomy creation and closure was assessed in a small series, and early closure of ileostomy has been suggested to reduce overall stoma-related morbidity and patient discomfort. In a randomized controlled trial of 186 patients, Alves et al. [31] reported similar overall surgical complication and re-operation rates in early (eight days) and late (60 days) ileostomy closure groups. However, site complications were more frequent (19% vs, 5%) with early closure. A meta-analysis reviewing four randomized controlled trials on 446 patients reported that anastomotic leak, anastomotic stenosis, and overall post-operative complications were similar between early and late closure. However, there was no particular conclusion on SSI rates in that study [32]. We preferred late closure after two months in both groups.

The recent intra-operative methods to prevent SSI include proper anti-microbial prophylaxis, anti-microbial sutures, incision irrigation, maintenance of normothermia, and proper glycemic control [33]. The most common intra-operative technique to prevent SSI is to irrigate the site with antiseptic solution. For this purpose, several solutions and antibiotics have been in use, but there is no evidence-based standard of practice [34]. A recent meta-analysis of 21 randomized controlled trials compared the effect of povidone–iodine solutions and non-povidone–iodine solutions (saline and antibiotics) and revealed that there is low-quality evidence that site irrigation with aqueous povidone–iodine solution decreases the SSI rate [35]. Antibiotic solutions had no beneficial effect. This meta-analysis includes no data on CHG solutions [35]. A Cochrane review performed by Normal et al. included 59 randomized controlled trials with 14,738 patients [36]. They compared incision irrigation with no irrigation (20 studies; 7,192 patients) and found no clear difference; antibacterial irrigation with non-antibacterial irrigation (36 studies; 6,136 patients) and low-certainty evidence in favor of antibacterial irrigation; two antiseptic agents of the same class (e.g., povidone–iodine with superoxidized water) (10 studies; 2,118 patients) and found no clear difference in the risk of SSI [36]. The subgroups of this review include several different site types and techniques, as well as different irrigation solutions tiered in the same group. There are few studies comparing CHG irrigation with other solutions to achieve a conclusion. This review

concluded that none of those results has certainty, and there is a need for new, better designed trials [36].

Chlorhexidine gluconate has long been in use as a potent antiseptic agent in pre-operative skin preparation [37]. In an in-vitro study, CHG solutions have been suggested to be more effective at eradicating *Staphylococcus epidermidis* with shorter exposure time from biofilm compared with povidone–iodine and antibiotic solutions [38]. In their meta-analysis of 19 studies comparing CHG with povidone–iodine, Privitera et al. [39] reported that pre-operative skin antisepsis with CHG reduced the SSI incidence (OR 0.70) and bacterial skin colonization (OR 0.45). Several studies have shown that 0.05% CHG solution can be used for antisepsis of tissues and surgical prostheses without causing adverse effects on site healing or granulation tissue formation [39]. However, there are limited published data on intra-operative incision irrigation with CHG. Our study evaluated the effect of incision irrigation with CHG on site complications, which has not been focused on before in the literature to our knowledge.

Intra-operative CHG irrigation prior to incision closure may offer a benefit over other antibiotic and saline solutions, which require a longer exposure. In an in-vitro pilot study, a five- to six-log reduction in microbial activity for both gram-negatives and gram-positive organisms was observed with 0.05% CHG irrigation at one and five minutes [40]. In our series, post-operative site complications, including seroma, incision dehiscence, and SSI were reduced significantly by 0.05% CHG irrigation. None of our patients had an adverse event associated with CHG. Earlier site healing was observed in the CHG group. Additionally, healing was assessed with an objective scoring performed by a blinded surgeon.

One should keep in mind that the degree of operative site contamination is often different for different surgeons; thus, the surgeon is one of the most important independent variables in incision infection after colorectal surgery. Our CHG group included a single surgeon's patients, which were compared with two other surgeons' patients. This non-randomized design is the major limitation of our study. Nevertheless, all primary surgeons were senior colorectal surgeons who have been working together for several years at Dokuz Eylul University Hospital. There was no difference between groups in the frequency of anastomotic leak.

Intra-operative site irrigation may contribute to decreased morbidity and costs. However, there are several irrigation practices regarding the type of solution, duration, and pressure of irrigation so that performing an objective comparison is difficult. A 0.05% CHG solution can be used safely, but there is a need for randomized and wider clinical trials to define the effect of irrigation on SSI.

Author Disclosure Statement

The authors declare no conflict of interest.

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