The Use of Collatamp G, Local Gentamicin-Collagen Sponge, in Reducing Wound Infection

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We conducted a retrospective study to examine the role of Collatamp G in reducing postoperative surgical site infection (SSI) in patients with different wound classes. Ninety-two patients (62 men and 30 women; mean age, 58 years; range, 29–88 years) who had undergone surgery between December 2009 and November 2011 in Tan Tock Seng Hospital and who had application of Collatamp G in their wound before closure were included in the study. The primary endpoint was the development of any superficial wound infection within 1 month postoperatively. Of 92 patients studied, 9 (10%) developed a superficial wound infection. Two of 43 patients with clean-contaminated wounds (5%), 2 of 19 with contaminated wounds (11%), and 5 of 30 with dirty-infected wounds (16%) developed infection. Use of the larger size Collatamp G (10 × 10 cm) also appears to have a lower incidence of SSI compared with the smaller Collatamp G (5 × 5 cm); 4% and 12%, respectively. Our data suggest that postoperative SSI was reduced in the group of patients with dirty-infected wound class. SSI appears to be decreased with use of the larger size Collatamp G.

Key words: Collatamp G – Gentamicin-collagen – Surgical site infection – Dirty infected – Wound class

Surgical site infection (SSI) is the second most common adverse event in hospitalized patients after adverse drug events.¹ Studies show that nearly 3% of all postoperative patients develop SSI, which prolongs hospital stay, extends the recovery period, and causes additional morbidity, pain, and in some

instances death.² Affected patients are as much as 60% more likely to spend time in an intensive care unit.³

Collatamp G (Schering-Plough, Stockholm, Sweden) is a gentamicin-impregnated collagen matrix that is used as a topical adjunct for perioperative

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antibiotic prophylaxis. In 1970, the National Nosocomial Infection Surveillance Survey was conducted to identify factors that played a role in postoperative wound infections,⁴ which led to the 1985 Center for Disease Control (CDC) guidelines for preventions of postoperative wound infection.⁵ The guidelines provided updated estimated postoperative rates of SSI: 1% to 5% for clean; 3% to 11% for clean-contaminated; 10% to 17% for contaminated; and over 27% for dirty.^{6,7} We conducted a retrospective study to examine whether Collatamp G reduces the incidence of postoperative SSI in patients with these wound classes.

Materials and Methods

We collected data from the medical records of patients who had Collatamp G applied intraoperatively at the department of General Surgery of a single institution, Tan Tock Seng Hospital. Standard sterilization and preparation procedures were followed as per our institution protocol.⁸ This includes using clippers for preoperative hair removal and following standardized prophylactic antibiotic guidelines consistent with international recommendations.

We classified all surgical procedures according to the CDC surgical wound classification system.⁵ Surgical sites are classified according to the level of contamination into class I (clean), class II (clean-contaminated), class III (contaminated), and class IV (dirty-infected). We conducted analysis of patients with clean-contaminated, contaminated, and dirty-infected wound classes as they would potentially benefit from antibiotic prophylaxis.

We maintained a separate registry of patients in whom Collatamp G was used. For each of the patient records, we collected the following information: age at surgery, sex, smoking status, diabetes mellitus status, American Society of Anesthesiologists (ASA) class status, wound class, surgical procedure, surgeon, size of Collatamp G used, perioperative antibiotic administration, and postoperative SSI. We stratified types of surgery into 4 groups: upper gastrointestinal, colorectal, skin and subcutaneous, or hepatobiliary. The primary endpoint was the development of any superficial wound infection within 1 month postoperatively. We evaluated the presence of superficial wound infection by reviewing electronic medical records and outpatient clinic notes on follow-up. We used the CDC/National Nosocomial Infection Surveil-

lance criteria for SSI in an effort to use standard criteria for SSI.⁵

Gentamicin–Collagen Sponge

The gentamicin–collagen sponge (Collatamp G, Schering-Plough, Stockholm, Sweden) used in this study consists of a matrix of purified bovine collagen type I impregnated with 2.0 mg/cm² gentamicin sulphate. The drug is released by a combination of diffusion and enzymatic breakdown of the collagen matrix, giving a high local concentration for at least 72 hours.⁹ The collagen matrix itself is fully resorbed within 1 to 7 weeks depending on the location (well-vascularized tissues versus bone cavities). Collatamp G is available in 5 × 5-cm or 10 × 10-cm sheets. It is cut into small strips that are applied in the subcutaneous layer or level of the sheath during wound closure.

Statistical Analysis

We summarized patient characteristics and study results using proportions and means with standard deviations (Table 1). We used Student's *t* test to compare continuous variables between groups. For categorical variables, we used χ^2 and Fisher's exact tests (when appropriate) to determine differences in proportions between groups. In addition, odds ratios were reported where appropriate.

We used multivariate logistic regression analyses to evaluate the relationship between the dependent variable (*e.g.*, development of SSI) and multiple independent variables (*e.g.*, smoking status) while eliminating covariates. All assumptions of logistic regression modeling were met. We included multiple cofounder variables in a multivariate model. All statistical analyses were carried out with Stata 10.0 (StataCorp, College Station, Texas) at 5% level of significance.

Results

Ninety-two patients (62 men and 30 women; mean age, 58 years; range, 29–88 years) who underwent surgery between December 2009 and November 2011 in Tan Tock Seng Hospital had application of Collatamp G in their wound before closure. Forty-three patients were in the clean-contaminated wound class, 14 patients were in the contaminated wound class, and 23 were in the dirty-infected wound class. Ten percent of all patients (9 of 92) developed a superficial wound infection. Five

Table 1 Baseline patient characteristics

	Clean Contaminated n=43	Contaminated n=19	Dirty Infected n=30	P value
Age				
Mean (years)	59 (28-85)	54 (29-78)	60 (27-88)	0.43
Gender				
Male	29	11	22	0.53
Female	14	8	8	
Comorbidity				
Diabetes	10	4	5	0.80
Smoking History				
Smoker	4	1	6	0.31
Size of Collatamp G				
5 x 5 cm	28	16	21	0.35
10 x 10 cm	15	3	9	
Type of Surgery				
Upper Gastrointestinal	24	4	11	0.01
Colorectal	6	9	15	
Skin and Subcutaneous Tissue	7	3	3	
Hepatobiliary	6	3	1	

percent of clean-contaminated wounds (2 of 43), 11% of contaminated wounds (2 of 19), and 16% of dirty-infected wounds (5 of 30) developed infection; $P = 0.23$.

We investigated the pattern of SSI rate after Collatamp G usage by comparing the incidence of SSI across different wound classes with conventional data in the literature (Fig. 1). The incidence of SSI

is 16% in dirty-infected wounds with Collatamp G use compared with 30% incidence of SSI without Collatamp G usage.⁷

To investigate the pattern of SSI after Collatamp G usage in subgroups of our study population, we conducted a subgroup analysis. We compared the incidence of SSI in patients who had undergone laparotomies with non-laparotomies. The propor-

Fig. 1 Comparison of incidence of SSI after usage of Collatamp G with known incidence of SSI in the literature.

Table 2 Multivariate logistic regression analysis of SSI rate

	Adjusted OR (95% C.I.)	p-value
Age		
≥ 70 (years)	Reference	-
< 70 (years)	0.26 (0.05-1.33)	0.11
Gender		
Female	Reference	-
Male	1.87 (0.29-12.03)	0.51
Smoking History		
Non Smoker	Reference	-
Smoker	0.38 (0.03-4.51)	0.44
Wound Class		
1: Dirty Infected	Reference	-
2: Contaminated	0.67 (0.10-4.61)	0.29
3: Clean Contaminated	0.43 (0.06-3.20)	0.41
Size of Collatamp G		
1: 10 x 10 cm	Reference	-
2: 5 x 5 cm	6.55 (0.51-84.42)	0.15
Type of Surgery		
1: Colorectal	Reference	-
2: Hepatobiliary	- (no SSI)	-
3: Skin and Subcutaneous Tissue	0.83 (0.06-10.83)	0.89
4: Upper Gastrointestinal	0.42 (0.06-3.13)	0.40

tion of patients with laparotomies who developed SSI was 11% (7 of 64) compared with non-laparotomies with an SSI of 7% (2 of 28); $P = 0.72$. We also stratified the incidence of SSI according to type of surgery performed. The SSI rates for colorectal surgery, upper gastrointestinal surgery, and skin and subcutaneous surgery were 16% (5 of 30), 8% (3 of 39), and 8% (1 of 13), respectively. There were no SSIs in our hepatobiliary operations ($n = 10$).

The size of Collatamp G used also appears to have an effect on SSI rate, with the proportion of patients with Collatamp G (10 × 10 cm) developing SSI being lower at 4% (1 of 27) compared with 12% (8 of 65) for Collatamp G (5 × 5 cm); $P = 0.23$.

We conducted a multivariate regression analysis to characterize SSI and potential risk factors (Table 2). We included the following parameters in the regression analysis: age, sex, smoking status, wound class, size of Collatamp G, and type of surgery, none of which are significant when added to the multivariate regression model.

Incidence of SSI in diabetics and smokers was also audited. Nineteen patients were diabetic, and

none developed SSI. Eleven patients were smokers, and only 1 developed SSI.

Discussion

SSI has been shown to add substantial cost to our health care system. In an earlier study from our institution by Liao *et al*,⁸ the mean estimated direct cost of extended hospital stays, nursing care, drugs, and dressing change for each patient with SSI was estimated to cost the hospital an additional SGD \$2160 (US \$1530) per patient. After implementing an SSI interventional bundle, it saved 2.6% ($n = 63$) of patients undergoing elective gastrointestinal and hernia operations from SSI. The estimated total cost savings by patients in this study over 2 years was about SGD \$136,080 (US \$97,200). Furthermore, SSI also carries significant emotional burden by affecting patient quality of life, increasing days away from work and decreasing productivity. Therefore, with significant benefits expected from the prevention of each SSI, we aimed to examine if Collatamp G could complement this SSI bundle and further lower SSI rates in our institution.

In earlier studies conducted on the use of Collatamp G in reducing SSI, Musella *et al*¹⁰ examined its use in prosthetic repair of groin hernia and concluded that it was effective in reducing SSI with 0.3% (1 of 301) in the Collatamp G group developing SSI compared with 2.0% (6 of 294) in the control group, ($P = 0.04$; Fisher exact test). However, this benefit in reduction of SSI was not reproduced in another study conducted by Anderson *et al*,¹¹ who examined the use of Collatamp G in pilonidal excision with midline suture. In this series, the SSI rate for the control group without Collatamp G was 26% (20 of 77) at 2 weeks follow-up, while the SSI rate for the intervention group with Collatamp G use was 22% (18 of 82); $P = 0.518$.

With these mixed results from earlier studies, we aimed to be selective in the use of Collatamp G and to identify the subgroup of patients who would benefit most from it in our study. This is especially important as the cost of Collatamp G is a consideration in our local setting, with Collatamp G (5×5 cm) and Collatamp G (10×10 cm) sheets costing SGD \$180 (US \$146) and SGD \$360 (US \$292), respectively. Our study aims to look at a broader spectrum of surgeries and comprises a varied mixture of abdominal and soft tissue surgeries.

Since data from our institution by Liao *et al*⁸ already demonstrated low SSI rates for clean and clean-contaminated wounds (0% and 1.1%, respectively, from the period of 2005 to 2007), we were interested in evaluating the effect of Collatamp G on other wound classes. Dirty-infected wounds have the most potential for benefiting from Collatamp G use since this group of patients are at the highest risk of developing SSI. In fact, the SSI rate for this group of patients with Collatamp G use was halved in our study compared with conventional data in the literature (15% and 30%, respectively).

Of interest, use of the larger size of Collatamp G (10×10 cm) appears to have a lower incidence of SSI compared with Collatamp G (5×5 cm); 4% and 12%, respectively). This could be related to dose-concentration effect of antibiotics in the wound. Future studies could be conducted to establish the correlation between size of the Collatamp G used and wound size, as this can guide surgeons on the appropriate choice of size of Collatamp G to use in order to maximize the cost-benefit ratio.

We also examined the effect of Collatamp G on well-established risk factors for SSI. Diabetes is considered an important risk factor for SSI after general surgery procedures.¹² In our study, none of the diabetic patients developed SSI after Collatamp

G use ($n = 19$). Similar to diabetics, smokers have well-described delays in primary wound healing.¹³ Prior studies have corroborated cigarette smoking as an important SSI risk factor after general surgical procedures.^{14,15} In our study, only 1 of 11 of smokers developed SSI. Our data suggest that patients with these 2 important risk factors for SSI have low incidence of SSI after Collatamp G usage, but a larger sample size is required to establish statistical significance.

In conclusion, our data suggest that the postoperative SSI rate was reduced in the group of patients with dirty-infected wound class, with a lower incidence of SSI being observed in patients who had larger sheets of Collatamp G placed intraoperatively. More data with a larger sample size can be conducted in a prospective study to determine the statistical relationship in this subgroup of patients with dirty-infected wound class and to determine whether SSI is affected by the size of Collatamp G used.

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