

An Evaluation of Peri-Operative Antimicrobial Use and Surgical Site Infection Rates in General Surgery

Sheryl A. Zelenitsky, Robert Chony and Rudy Danzinger

ABSTRACT

The prescribing, delivery, and effectiveness of surgical prophylaxis were assessed in 201 general surgery patients. Antimicrobials were ordered prior to 156 (73%) of 213 operations. For biliary, colorectal, hernia, breast, and head and neck procedures, prophylaxis was used in 90% (44/49), 100% (46/46), 73% (22/30), 9% (2/22) and 22% (4/18) of cases, respectively. Antimicrobial selection was inappropriate in 15% (23/156) of cases. The administration of 28% (67/238) of prophylactic doses was either not recorded or occurred at inappropriate times relative to the time of incision. Antimicrobial therapy was continued post-operatively in 18% (28/156) of cases for treatment of existing infection or surgical complication. The duration of prophylaxis was inappropriately prolonged following 41% (14/34) of colorectal and 33% (31/94) of other operations. Prophylactic antimicrobials were associated with significant adverse effects in 3.2% (5/156) of patients. Twelve surgical site infections (SSIs) were diagnosed during hospitalization, two were identified upon readmission, and an additional seven were identified during post-discharge follow-up. A high incidence of SSIs observed following colorectal operations was associated with low doses and inappropriate timing of prophylactic antimicrobials.

Key Words: antibiotics, prophylaxis, surgical site infection

RÉSUMÉ

La prescription, l'administration et l'efficacité de la prophylaxie chirurgicale ont été évalués chez 210 patients subissant une chirurgie générale. Des antibiotiques ont été prescrits avant l'opération pour 156 (73 %) des 213 chirurgies. On a eu recours à l'antibiothérapie prophylactique dans les proportions suivantes, pour chaque type de chirurgie : biliaire 90 % (44/49); colorectale 100 % (46/46); herniaire 73 % (22/30); du sein 10 % (2/20); cervico-crânienne 22 % (4/18). Dans 15 % des cas (23/156) le choix de l'antibiotique était inadéquat. De plus, l'administration de doses prophylactiques 28 % (67/238) n'a soit pas été documentée, soit été effectuée au mauvais moment par rapport au moment où l'incision a eu lieu. L'antibiothérapie a été poursuivie dans 18 % (28/156) des cas pour le traitement d'une infection existante ou due à une complication chirurgicale. La durée de l'antibiothérapie prophylactique a été indûment prolongée dans 41 % (14/34) des cas de chirurgie colorectale et dans 33 % (31/94) des autres chirurgies. L'antibiothérapie prophylactique

a été associée à des réactions indésirables graves chez 3,2 % (5/156) des opérés. Au cours de l'hospitalisation, on a diagnostiqué 12 infections dans la région opérée, dont deux l'ont été lors de leur réadmission et sept autres au cours des suivis après leur congé. On a signalé une fréquence élevée d'infection dans la région opérée lorsque les antibiotiques étaient administrés à faible dose ou à un moment inopportun.

Mots clés : antibiotiques, prophylaxie, infection dans la région opérée

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INTRODUCTION

Variability in the prescribing and delivery of pre-operative antimicrobials can significantly influence the efficacy, toxicity and cost associated with surgical prophylaxis. Nevertheless, inconsistencies in antimicrobial selection, dose, timing, and duration of therapy within institutions have been documented.^{1,2} Crossley and colleagues reported significant variability in the administration of prophylaxis to 1021 patients who had undergone obstetric, gynecologic, orthopedic, urologic, or general surgical procedures.¹ Prophylaxis was administered more than four hours prior to surgery in 15% of cases, within four hours of surgery in 41%, intra-operatively in 16%, and post-operatively in 28%. The mean duration of prophylaxis varied with surgical speciality ranging from 53 to 112 hours. Classen et al

Sheryl A. Zelenitsky, PharmD, is Assistant Professor, Faculty of Pharmacy, University of Manitoba, Winnipeg, Manitoba.

Robert Chony is a Bachelor of Science in Pharmacy Student, Faculty of Pharmacy, University of Manitoba.

Rudy Danzinger, MD, FRCSC, is Head, Department of Surgery, St. Boniface General Hospital, Winnipeg, Manitoba, and Professor, Faculty of Medicine, University of Manitoba.

Address Correspondence to: Dr Sheryl Zelenitsky, Assistant Professor, Faculty of Pharmacy, University of Manitoba, Winnipeg, Manitoba R3T 2N2

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demonstrated similar variability in the timing and duration of prophylaxis in 2847 patients who had undergone hysterectomies, cholecystectomies, bowel resections, gastric bypasses, or orthopedic operations.²

Standardization programs can improve the prescribing and delivery of prophylaxis, reduce costs, and improve patient outcomes. Significant cost savings have been documented by making the appropriate selection of antimicrobial prophylaxis for specific surgical procedures.^{3,4} Evans and associates utilized computer surveillance to detect prolonged courses of prophylaxis.⁵ Medication profiles were interfaced with microbiological data in order to identify extended courses of antimicrobials in cases without evidence of infection. In a subsequent prospective trial, the same investigators demonstrated that the surveillance program impacted positively on clinical outcomes by reducing post-operative infections.⁶

The purpose of this study was to evaluate the prescribing, delivery, and effectiveness of prophylaxis for general surgery at a tertiary-care teaching hospital. This project was undertaken to identify any deficiencies in surgical prophylaxis and develop mechanisms to improve the process.

METHODS

Data Collection

All patients admitted to general surgery during a 10-week period were considered for inclusion. Only those who did not undergo a procedure or were receiving antimicrobials prior to surgery were excluded. Information was collected during hospitalization from medical charts, attending surgeons, house staff, and patients. Patient demographics were recorded including age, weight, date of admission, and length of stay. A medical history of drug allergies, diabetes mellitus, malignancy, chronic renal failure, and corticosteroids or immunosuppressant therapy was also obtained. The condition requiring surgery was described and the date, time, classification, duration, and complications of the operation were documented.

The administration of prophylactic antimicrobials such as dose, route, timing, duration of therapy, and adverse effects was detailed. Post-operative courses of antimicrobials for the treatment of surgical site or other infections were documented. During hospitalization, the diagnosis of surgical site infections (SSIs) was based on the definition

of nosocomial SSIs by the Centers for Disease Control.⁷ Local (erythema, pain, purulent drainage) and systemic (fever, elevated white blood cell count) signs of infection were recorded daily. Microbiological results were documented when available.

Since SSIs can occur up to 30 days post-operatively, patients were contacted by telephone after discharge. A SSI was documented when the patient described local signs of infection which required treatment with systemic antibiotics.

Data Analysis

Data were collected and entered into a relational data base (FoxPro^R) for analysis. Surgical cases were categorized into head and neck, non-cardiac thoracic, gastro-duodenal, biliary, colorectal, appendiceal, clean (hernia, breast) or other procedures. The indications for prophylaxis were assessed according to guidelines developed from an extensive review of the literature (Table I).

Similarly, antimicrobial selection was reviewed and compared to the recommendations outlined in Table II. If alternate therapies were selected, rationale and support for the drug, dose, and route were evaluated. The appro-

Table I: Proposed recommendations: indications for surgical prophylaxis.

Surgical category	Prophylaxis is indicated for:	Prophylaxis is controversial for:
Head and neck	clean-contaminated procedures with incision of oral or pharyngeal mucosa ^{8,9}	clean procedures ¹⁰
Non-cardiac thoracic	pulmonary resection (lobectomy, pneumonectomy) ^{11,12}	closed-tube thoracostomy for trauma ¹³
Gastro-duodenal	high risk procedures ¹⁴ (gastric-bypass ¹⁵ ; percutaneous endoscopic gastrotomy ¹⁶ ; acid suppression, obstruction ¹⁷ ; malignancy, hemorrhage)	low risk procedures
Biliary	high risk procedures with bactobilia (age >60, acute cholecystitis, obstructive jaundice, common bile duct stones) ^{18,19}	low risk procedures ^{20,21}
Colorectal	all procedures ^{22,23}	
Appendiceal	all procedures ²⁴ ; post-operative treatment is required for complicated cases with perforation or gangrene ^{25,26}	
Clean		clean hernia, breast procedures ^{27,28,29}

priateness of antimicrobial selection was determined and variability in regimens was assessed according to surgical procedure.

The timing of prophylaxis relative to the time of incision was calculated. Pre-operative doses administered within one hour of surgery were considered ideal, whereas, those delivered between one and two hours prior to incision were defined as acceptable.²

The duration of prophylaxis was documented for each case. Single dose prophylaxis was appropriate for non-cardiac thoracic,¹² gastroduodenal,^{32,33} and biliary procedures.^{34,35,36} For prolonged operations, additional intra-operative doses were considered appropriate. Multiple dose regimens not exceeding 24 hours were acceptable for head and neck,³⁷ colorectal,^{38,39} and uncomplicated appendiceal operations.^{24,40} If the surgery identified existing infection or resulted in complications requiring antimicrobial treatment, post-operative therapy was considered treatment, not prophylaxis. Prolonged courses, however, in patients without microbiological or clinical evidence of infection were reported as inappropriate. The cost and number of excess doses associated with extended prophylaxis were also calculated.

SSI rates during hospitalization and after discharge were calculated according to surgical category. Post-operative infections and potential risk factors were closely examined for biliary and colorectal procedures, whereas, data interpretation was limited by small numbers in other surgical categories. Potential risk factors including obesity (> 20% of ideal body weight), diabetes mellitus,

chronic renal failure, malignancy, immunosuppressant or corticosteroid therapy, duration of surgery, surgical complications, and inappropriate prophylaxis were compared between patients with and without SSIs using the Fisher's exact test ($\alpha = 0.05$).

RESULTS

Two-hundred and one patients who underwent 213 operations performed by 10 surgeons were enrolled into the study. The most common were biliary procedures (49) followed by colorectal (46), hernia (30), breast (22), head and neck (18), appendiceal (11), laparotomy (9), noncardiac thoracic (6), gastroduodenal (5), and other (17) operations.

Indication for prophylaxis: Pre-operative antimicrobials were ordered for 156 (73%) of the 213 operations. Ninety percent (44/49) of patients who underwent biliary surgery and 100% (46/46) of those who had colorectal operations received prophylaxis. Seventy-three (22/30) percent of patients who underwent hernia repair, and 9% (2/22) of patients who had breast surgery received pre-operative antimicrobials. Prophylaxis was administered for clean-contaminated head and neck operations, but not for clean procedures without incision of the oral or pharyngeal mucosa. All appendectomies, abdominal laparotomies, and gastroduodenal operations were preceded by the administration of prophylaxis.

Antimicrobial selection: Cefazolin (1 gram) was selected for 59% (26/44) of prophylactic regimens administered for biliary surgery. In an additional 30% (13/44) of cases, alternate regimens including piperacillin, cefuroxime, cefotaxime or ampicillin plus an aminoglycoside were used. Inadequate coverage was provided by single therapy clindamycin, metronidazole, or ampicillin in 11% (5/44) of cases.

All patients who underwent colorectal surgery received parenteral prophylaxis. Oral antimicrobials alone or in combination with parenteral therapy were not used. Prophylaxis consisted of an aminoglycoside (gentamicin or netilmicin) plus metronidazole with or without ampicillin for 76% (35/46) of colorectal operations. The mean aminoglycoside dose was 80 mg or 1.1 mg/kg. Alternate regimens including 1 gram doses of cefoxitin or cefazolin plus metronidazole were selected in an additional 13% (6/46) of cases. Single therapy cefazolin or metronidazole or an aminoglycoside plus vancomycin provided suboptimal colorectal prophylaxis in 11% (5/46) of cases.

Table II: Proposed recommendations: antimicrobial selection^a for surgical prophylaxis.

Surgical categories	The Medical Letter ³⁰	Alternate regimens ³¹
Head & neck (clean-contaminated)	cefazolin 1-2g or clindamycin 600-900mg	gentamicin + clindamycin,
Non-cardiac thoracic	cefazolin 1-2g	
Gastroduodenal (high-risk)	cefazolin 1g	gentamicin + clindamycin
Biliary (high-risk)	cefazolin 1g	gentamicin ± metronidazole
Colorectal	neomycin + erythromycin ^b or cefoxitin 1g or cefotetan 1g	neomycin + metronidazole ^c , gentamicin + metronidazole/clindamycin
Appendiceal (uncomplicated)	cefoxitin 1g or cefotetan 1g	gentamicin + metronidazole/clindamycin

^a intravenous doses unless otherwise indicated

^b after appropriate catharsis, 1g oral doses of neomycin and erythromycin at 1300, 1400, and 2300 hour the day before an 0800 hour operation

^c oral lavage solution for 4-6 hours until effluent is clear, followed by 2g oral doses of neomycin and metronidazole at 1900 and 2300 hour one day preoperatively

Antimicrobial selection for the remaining operations was appropriate. Prophylaxis for hernia, breast, and head and neck surgery consisted of cefazolin (1 gram). Clindamycin or vancomycin were selected for a small number of patients who had histories of penicillin allergy. For appendectomy prophylaxis, cefoxitin, cefazolin plus metronidazole, or an aminoglycoside plus metronidazole were selected.

Timing of prophylaxis: Figure 1 depicts the timing of all antimicrobial doses which were ordered pre-operatively. Thirty-five percent (83/238) of doses were given within one hour and 37% (88/238) were within one and two hours prior to surgery. The remaining doses were either not recorded or were administered at times greater than two hours prior to incision, during surgery, or post-operatively.

Duration of prophylaxis: Colorectal operations were separated from other procedures for analysis because of the greater tendency to continue antimicrobials post-operatively. Following 12 (26%) colorectal procedures, antimicrobial therapy was continued for spillage, chronic fistulas, gangrenous bowel or perforation. Excluding patients requiring treatment, single and multiple dose prophylactic regimens were selected in 9% (3/34) and 91% (31/34), respectively. The duration of prophylaxis was variable ranging from 12 to 96 hours postoperatively (median 30 hours). In 41% (14/34) of colorectal cases, the duration of prophylaxis was determined to be inappropriate as it exceeded 24 hours without evidence of infection.

Sixteen patients (15%) who underwent non-colorectal procedures required antimicrobial therapy post-operatively for existing infection or surgical complication. Single dose prophylaxis was selected in 57% (54/94) of remaining cases. Multiple dose regimens not exceeding

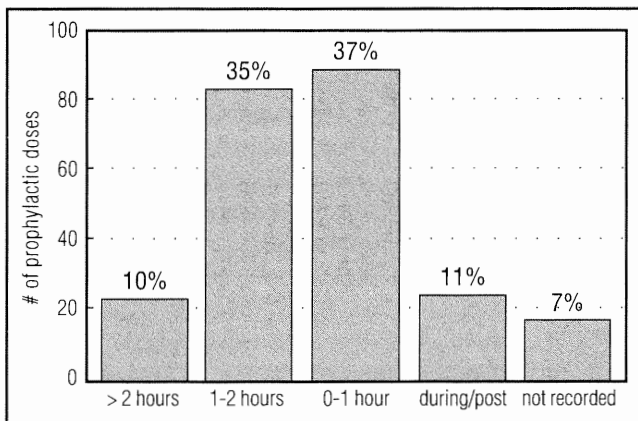


Figure 1: Timing of 238 prophylactic doses (>2 hours = greater than 2 hours prior to incision, 1-2 hours = within 1 and 2 hours prior to incision, 0 - 1 hours = within 1 hour of incision, During/post = during or after surgery, Not recorded = dose not recorded in patient chart).

24 hours were appropriately used in cases involving clean-contaminated head and neck procedures or uncomplicated appendectomies. The duration of prophylaxis following 33% (31/94) of non-colorectal operations was determined to be inappropriate.

Overall, inappropriately prolonged prophylaxis was identified in 35% (45/128) of general surgery cases. This translated into the administration of approximately 1800 unnecessary antimicrobial doses annually and an estimated drug cost of \$6500.

Adverse effects: Significant adverse effects were identified in 3.2% (5/156) of patients who received prophylactic antimicrobials. Two hypersensitivity reactions including anaphylaxis and urticarial rash occurred following a pre-operative cefazolin dose in patients without a history of allergy. *Clostridium difficile* infections were diagnosed in three patients who had diarrhea and a positive result for *Clostridium difficile* toxin.

Surgical site infection rates: Figure 2 illustrates SSI rates according to surgical procedure. Twelve SSIs were diagnosed during hospitalization and two were identified upon re-admissions related to a surgical site complication. Ninety percent of the 181 patients eligible for follow-up were interviewed between 25 and 35 days post-operatively. Patients not contacted by telephone included those who refused consent, could not communicate verbally, or were still hospitalized. The follow-up identified seven additional SSIs which developed after discharge and required treatment with oral antibiotics.

SSI rates for low and high risk biliary procedures were 3.7% (1/27) and 13.6% (3/22), respectively. One SSI was

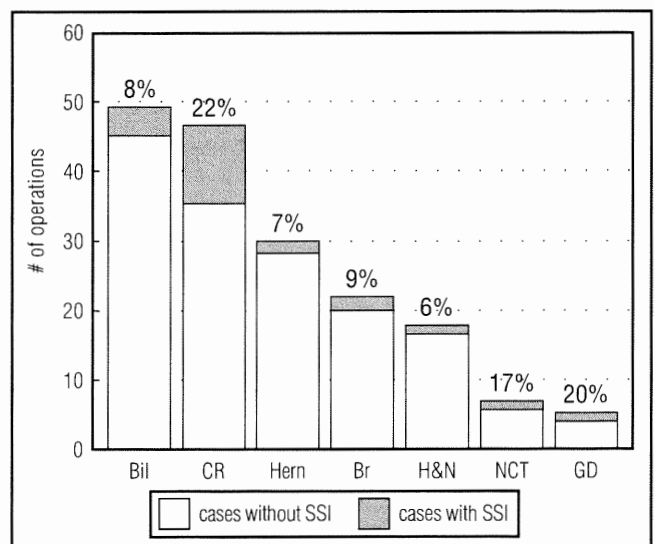


Figure 2: Surgical site infection (SSI) rates according to surgical category. Bil = Biliary, CR = Colorectal, Hern = Hernia, Br = Breast, H+N = Head and Neck, NCT = Non-Cardiac Thoracic, GD = Gastroduodenal

diagnosed during hospitalization, one required re-admission and the remaining were identified after discharge. No differences in risk factors were detected between patients who did and did not develop SSIs, however, the numbers were relatively small. One patient was among the 10% who did not have prophylaxis, whereas, the remaining patients received pre-operative antimicrobials. The patient who developed an infectious complication and was readmitted received inadequate prophylaxis with metronidazole alone.

The infection rates in patients who underwent colorectal surgery were 17% (8/46) during hospitalization, and 22% (10/46) at 30 days post-operatively. No differences were observed in the presence of obesity, diabetes mellitus, chronic renal failure, malignancy, immunosuppressant therapy, corticosteroid therapy, duration of surgery, or surgeon (p values > 0.05). A significant difference, however, was detected in the timing of prophylaxis. Timing was inappropriate in 70% (7/10) of cases which developed SSIs, and in 25% (9/36) of those which did not have post-operative infections (p value = 0.02).

DISCUSSION

Indication for prophylaxis: Although the benefits of prophylaxis for some operations is well established, antimicrobials are also associated with adverse events, the development of superinfections and bacterial resistance. Based on the relative benefits and risks, prophylaxis is indicated for clean-contaminated head and neck, high risk gastroduodenal, high risk biliary, and colorectal operations (Table I). During this study, pre-operative antimicrobials were ordered for all patients who underwent these procedures.

The benefit of prophylaxis for low risk biliary (including laparoscopic), hernia and breast procedures is debatable. Ninety percent of patients who underwent biliary surgery received prophylaxis with no predilection for high versus low risk or open versus laparoscopic procedures. Since post-operative infections are associated with the presence of bactobilia, prophylaxis has been recommended for high risk patients greater than 60 years, with fever, acute cholecystitis, common bile duct stones, or obstructive jaundice.³⁰ The correlation, however, of these characteristics with the presence of bactobilia and risk of infection has been challenged.^{19,20} It was the authors' opinion and recommendation that the use of prophylaxis for all biliary operations is cautious but not inappropriate. In response to the results of this project and current controversy, a study to assess prophylaxis for laparoscopic biliary operations is being considered.

During this study, the use of prophylaxis for clean operations was variable. Antimicrobials were administered prior to 73% (22/30) of hernia repairs, even though

90% were classified as clean operations. On the other hand, few patients who underwent breast surgery received prophylaxis. The benefit of pre-operative antimicrobials for clean procedures is controversial. One prospective study demonstrated a statistically significant reduction in all post-operative infections, however, there was no difference in SSIs.²⁷ The absolute reduction in infection rates was relatively small and the benefits versus potential risks of antimicrobial prophylaxis were not assessed. A subsequent observational study of over 3,000 patients concluded that prophylaxis was most beneficial in high risk patients.²⁸ Since SSI rates following clean surgery are low without pre-operative antimicrobials, the benefits of prophylaxis do not outweigh the risks for uncomplicated, clean cases. It was recommended that only high risk patients with a predisposition to infection receive prophylaxis.

Antimicrobial selection: Antimicrobial selection should be based on spectrum of activity, pharmacokinetics, adverse effects, and cost. Cefazolin is suggested as first line prophylaxis for biliary surgery.³⁰ In situations where bactobilia may involve anaerobic organisms, metronidazole can be added to broaden the spectrum. Although cefazolin was selected for 59% (26/44) of biliary procedures, it could have been used in an additional 34% (25/44) of cases. Equally efficacious but more expensive prophylaxis was provided by piperacillin, cefuroxime, cefotaxime, or an aminoglycoside plus metronidazole. To ensure cost-effective biliary prophylaxis, it was recommended that antimicrobial selection include cefazolin for all non-allergic patients.

Although oral neomycin and erythromycin is often recommended as first line colorectal prophylaxis, a number of alternate intravenous, oral or combined regimens are supported in the literature (Table II). During this study, preference for parenteral prophylaxis over oral regimens was observed. Reasons for not selecting oral antimicrobials included same day admissions and a high incidence of gastrointestinal intolerance associated with the oral regimens. When parenteral antimicrobials alone are selected for prophylaxis, the dose and timing are extremely important in maintaining tissue concentrations throughout surgery. It was the authors' opinion and recommendation that pre-operative aminoglycoside doses of 1.5 to 2 mg/kg be administered and that intra-operative doses be used depending on the timing and duration of surgery.

Timing of prophylaxis: The timing of pre-operative doses is important in sustaining tissue concentrations during surgical contamination. In addition, the administration of intra-operative doses may be required to maintain concentrations during prolonged procedures. Stone and associates demonstrated that wound infection rates were significantly lower in patients who received pre-operative

versus post-operative antimicrobials.⁴¹ Classen and colleagues correlated SSI rates with timing and demonstrated fewest infections when prophylaxis was administered within two hours prior to incision.² Although parenteral doses within two hours are acceptable, timing within one hour of surgery is optimal.⁴²

During this study, 28% of all prophylactic doses were not recorded or were administered at inappropriate times. In addition, a number of these doses were identified in patients who developed SSIs following colorectal operations. Shared responsibility of antimicrobial administration among nurses, house staff, surgeons, and anesthesiologists may have accounted for some of the missed or poorly timed doses. Following extensive inservices with pharmacy, medicine, and nursing, a coordinated effort to standardize the timing of prophylaxis was initiated.

Duration of prophylaxis: There is varying support for the efficacy of single versus multiple dose prophylaxis according to surgical category. As previously mentioned, the efficacy of single dose prophylaxis is established for non-cardiac thoracic, gastroduodenal, and biliary procedures. Although single dose regimens are controversial for operations involving the head and neck (clean-contaminated), appendix, colon, and rectum, there is no support for prophylaxis to exceed 24 hours in uncomplicated cases.^{42,43,44} Excluding those requiring treatment, 35% (45/128) of all general surgery patients received prolonged courses of antimicrobials. Pre-operative orders written for antimicrobials to continue for 24 to 48 hours after surgery may have accounted for the prolonged prophylaxis after colorectal surgery. Based on these results and current controversy, an investigation of single versus multiple dose prophylaxis for colorectal surgery is underway.

Surgical site infection rates: This study emphasized the importance of post-discharge surveillance when determining SSI rates. One-third (7/21) of all infections were identified during the follow-up assessment, a majority of which occurred in patients who underwent laparoscopic cholecystectomies, hernia repairs, or breast operations requiring short hospital stays. Although the limitations of verbal follow-up may have resulted in conservative estimates, traditional surveillance would have significantly underestimated SSI rates.

In this study, the infection rates after biliary surgery were similar to the 5% for clean procedures, and 7-20% for complicated operations described in the literature.⁴⁵ The SSI rate observed in patients who underwent colorectal operations, however, was higher than the 5-10% which is suggested.⁴⁵ As a result, all colorectal cases were reviewed to detail the development of infection, identify potential risk factors and, perhaps, explain the high rate of SSIs. Antimicrobial selection which consisted

of metronidazole alone was inappropriate in one patient who developed infection following colorectal surgery. The remaining SSIs were identified in cases where prophylaxis with an aminoglycoside plus metronidazole or cefoxitin should have provided adequate coverage. As discussed previously, however, low aminoglycoside doses and poor tissue concentrations during surgery could have predisposed patients to post-operative infections. Two out of three obese patients developed an SSI after 1 gram of cefoxitin preoperatively, potentially signifying inadequate doses in these patients. The short half-life of cefoxitin (45 minutes in patients with normal renal function) makes the pre-operative dosing and timing of this antimicrobial even more critical.

The association between inappropriate timing of prophylaxis and the development of SSIs following colorectal operations was the most notable. In 35% of cases, antimicrobial administration was not recorded or occurred at unacceptable times. The SSI rates in these patients versus those who received appropriately timed prophylaxis were 44% (7/16) and 10% (3/30), respectively. Although based on retrospective analysis, the correlation between the inappropriate prescribing and delivery of prophylaxis and the development of SSIs supports the need for standardization and ongoing surveillance. ☒

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