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Mono- or Poly- Antimicrobial Prophylaxis in Colorectal Surgery

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Abstract

Objective: **The use of prophylactic antibiotics in colorectal surgery is well established. Type of antibiotics, however, varies significantly among surgeons. The aim of this study was to determine whether mono-antimicrobial regimen is as effective as poly-antimicrobial regimen in the prevention of surgical wound infections following elective colorectal cancer surgery.**

Materials and Methods: **The medical records of 56 patients with colorectal cancer undergoing elective oncological resection from January 2004 to September 2006 at Siriraj Hospital, Bangkok, were retrospectively reviewed. Patients were divided into two groups according to the regimen of prophylactic intravenous antibiotics; group A: monotherapy (cefminox-Meicelin®) and group B: polytherapy (ceftriaxone plus metronidazole). The duration of antibiotics administration was up to 24 hours in colonic surgery and up to 3 days in rectal surgery. Patient characteristics and rate of wound infection within 30 days after the operation were compared between the two groups.**

Results: **This study included 25 males and 31 females, with a mean age of 63 years (range 27-86). There were 18 patients in group A and 38 patients in group B. There was no significant difference in patient characteristics between the two groups. Overall rate of wound infection was 14.3%. Rate of wound infection was not significantly different between the two groups (group A 11.1% vs group B 15.8%, P = 1.00). No adverse drug reaction was found in this study.**

Conclusions: **Based on this study, there was no significant difference in the rate of wound infection following elective colorectal cancer surgery with mono-antimicrobial regimen, compared to that with poly-antimicrobial regimen. Thus, single drug regimen could be a feasible alternative in antibiotic prophylaxis for the prevention of wound infection following elective lower gastrointestinal tract surgery.**

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Introduction

The use of prophylactic antibiotics in colorectal surgery is well established as it significantly reduces the incidence of surgical wound infection. According to the Centers for Disease Control and Prevention (CDC) guideline in 1999[1], prophylactic antibiotics should have a bacteriocidal activity against the most probable intraoperative contaminants. In the case of colorectal surgery, expected pathogens are both aerobic and anaerobic organisms, mainly gram-negative bacilli and Bacteroides fragilis. Therefore, the antibiotics selected should be effective against all of them.

Practically, type of prophylactic antibiotics could vary significantly among surgeons[2]. Some prefer combined administration of two antibiotics (poly-antimicrobial regimen or polytherapy), whereas some prefer administration of single antibiotic (mono-antimicrobial regimen or monotherapy). Although monotherapy has been reported to be equivalent in safety and efficacy to polytherapy for antibiotic prophylaxis, there is very limited study regarding this subject in Thailand, particularly in major colorectal operations.[3]

Ceftriaxone, one of the third generation cephalosporin, offers broad-spectrum antimicrobial coverage with activity against gram-positive and gram-negative bacteria. It is one of the most common prophylactic antibiotics used in intra-abdominal surgery because of its bacteriocidal activity, long half life, easy administration and lack of nephrotoxicity. However, ceftriaxone does not have an activity against anaerobes. Thus, it is usually used in combination with metronidazole for lower gastrointestinal surgery.[4,5] Meanwhile, the new generation cephalosporin, cefminox (Meicelin®, Thai Meiji Pharmaceutical, Thailand) meets the requirement of a single broad-spectrum antibiotic being active against a wide range of gram-positive, gram-negative and anaerobic bacteria.[6] Therefore, it has been chosen to be used as a mono-antimicrobial regimen for antibiotic prophylaxis in colorectal surgery, and to be compared with a poly-antimicrobial regimen (ceftriaxone plus metronidazole).

The aim of this study was to determine whether mono-antimicrobial regimen was as effective as poly-antimicrobial regimen in the prevention of surgical wound infections following elective colorectal cancer surgery.

Materials and Methods

Medical records of patients with colorectal cancer undergone elective oncological resection between January 2004 and September 2006 at the Department of Surgery, Faculty of Medicine Siriraj Hospital, Bangkok, Thailand were reviewed. The enrollment criteria included patient receiving either cefminox or ceftriaxone plus metronidazole as prophylactic antibiotics. Patients were excluded if they had non-primary wound closure, underwent emergency operations or died within the first 48 hours after surgery. Patients with document of intraoperative gross contamination resulting in receiving longer period of antibiotics administration (therapeutic intention) were also excluded. Written informed consent was obtained from all patients.

All patients with rectal cancer and most patients with colon cancer underwent preoperative mechanical bowel preparation. Prophylactic intravenous antibiotics, either cefminox 1 gm or ceftriaxone 1 gm plus metronidazole 500 mg, were administrated by anesthesiologist after induction of general anesthesia. In case of operation time longer than 4 hours or with massive blood loss, additional dose of antibiotics may be given during the operation. Standard oncological resection was performed either laparoscopically or through open approach. Duration of antibiotics administration was determined by the surgeon's discretion, mostly up to 24 hours in colonic surgery and up to 3 days in rectal surgery. Wound infection was defined based on CDC criteria.[7]

Patients with surgical wound infection were discharged after the wound was well controlled and could be managed in the outpatient setting safely. All patients were scheduled for follow-up at 30 days postoperatively.

The data collected included age and gender, body mass index (BMI), American Society of Anesthesiologist (ASA) status, location of the tumor and the development of wound infection. Patients were divided into two groups according to the regimen of intravenous antibiotics administration; group A: monotherapy (cefminox - Meicelin®) and group B: polytherapy (ceftriaxone plus metronidazole).

All data were prepared and compiled using SPSS software (version 10.0 for Windows). Mean and standard deviation were assessed. The Kolmogorov-

Samirnov test was used to test for the pattern of data distribution. Unpaired t-test was used to compare data between the two groups when they were in normal distribution pattern. Mann-Whitney U test was used when this was not the case. Pearson chi-square test or Fisher's exact test was used for categorical data. A P-value of less than 0.05 was considered statistically significant.

Results

This study included 25 males and 31 females with a mean age of 63 years (range 27-86). There were 18 patients in group A and 38 patients in group B. Patient characteristics in both groups were well-matched (Table 1). Overall rate of wound infection was 14.3%. The rate of wound infection was not significantly different between the two groups (group A 11.1% vs group B 15.8%, P = 1.00). No adverse drug reaction was found in this study.

Discussion

Wound infection is a common but potentially preventable complication following colorectal surgery. Administration of prophylactic antibiotics inhibits the growth of contaminating bacteria, thus reducing rate of wound infection.[8] However, usage of antibiotics could encourage the emergence of resistant strains of organisms, especially Clostidium difficile and methicillin-resistant Staphylococcus aureus.[9] Therefore, the ideal prophylactic antibiotics should cover common pathogens, but has a minimal effect on the patient's normal flora and has minor adverse drug reactions. Cephalosporins meet the aforementioned principles, therefore, many guidelines have recommended them as a first line agent.[10] However, many cephalosporins do not have an activity against anaerobes. Thus, they are usually used in combination with metronidazole for lower gastrointestinal surgery.[4,5]

Table 1 Comparison of patient characteristics and rate of wound infection between monotherapy group and polytherapy groups. Values were given as number (percentage) or mean ± SD.

	Group A: Monotherapy (n = 18)	Group B: Polytherapy (n = 38)	P-value
Age (years)	61.9 ± 12.2	3.4 ± 13.4	0.69
Female	13 (72)	18 (47)	0.14
BMI (kg/m^2)	20.9 ± 3.8	22.1 ± 3.8	0.26
ASA status	2.0 ± 0.6	1.9 ± 0.5	0.41
Tumor location			0.68
colon	11 (61)	21 (55)	
rectum	7 (39)	17 (45)	
Wound infection	2 (11.1)	6 (15.8)	1.00

Considering the convenience of drug administration and the concern of drug compliance, the current trend toward the use of broad-spectrum single drug for antibiotic prophylaxis in colorectal surgery has continued. Our findings suggested that there was no significant difference in the rate of wound infection between mono- and poly- antimicrobial regimen. Several studies have demonstrated that single drug regimen is equivalent in safety and efficacy to combined drug regimen for antibiotic prophylaxis in elective colon and rectal surgery.[11-13] A prospective randomized trial of 422 patients in Germany revealed that three different types of antibiotics (ampicillin/sulbactam, cefoxitin and piperacillin/ metronidazole) are of equal value.[11]

A systematic review of 147 randomized controlled trials regarding antimicrobial prophylaxis in colorectal surgery confirms that the use of antimicrobial prophylaxis is effective for the prevention of surgical wound infection without any significant difference in the rate of wound infections among several different regimens,[14] providing that such intravenous antibiotics are given within 30-60 minutes before the incision and have a spectrum activity against aerobic and anaerobic pathogens of the lower gastrointestinal tract.

When the efficacy and safety of different prophylactic antibiotics are not significantly different, the cost and ease of use become more important and more considerable. The cost of antibiotic prophylaxis could be reduced by many means such as using single-dose or short-term drug regimen instead of inappropriate prolonged administration, using efficacious monotherapy instead of a combination of two or more antibiotics that need to be administered separately.[15,16]

Some limitations of the present study should be addressed. Firstly, data were collected retrospectively, relying on accurate and complete documentation of antibiotic prophylaxis and incidence of surgical wound

infection in patient notes. Thus, the validity of the results may also be affected by the incomplete data. Secondly, this study included a relatively small sample size; therefore, further prospective studies with a larger number of patients are required and cost-effectiveness among different mono- and poly-antimicrobial regimens in Thailand might be evaluated.

Conclusion

Our findings revealed that there was no significant difference in the rate of wound infection following elective colorectal cancer surgery between mono- and poly-antimicrobial regimens. Thus, single drug regimen could be a feasible alternative in antibiotic prophylaxis for the prevention of wound infection following elective lower gastrointestinal tract surgery.

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