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Original Research

The effects of preoperative oral antibiotic use on the development of surgical site infection after elective colorectal resections: A retrospective cohort analysis in consecutively operated 90 patients

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HIGHLIGHTS

- This study was performed in patients undergoing elective colorectal resection.
- The influence of oral antibiotic use with mechanical bowel preparation (MBP) on surgical site infection was mainly evaluated.
- The duration and cost of hospitalization were also evaluated in these patients.
- The duration and cost of hospitalization were also evaluated in these patients.
- The study group included patients who were administered with both oral antibiotics (gentamycin, metronidazole and bisacodyl) and MBP.
- The control group consisted of patients who received MBP only.
- Patients receiving oral antibiotics demonstrated a lower rate of wound infections and shorter hospital stay.
- Patients treated with oral antibiotics showed similar rates for anastomotic leakage with significantly lower total hospital charges.

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ABSTRACT

Purpose: The influence of oral antibiotic use together with mechanical bowel preparation (MBP) on surgical site infection (SSI) rate, length of hospital stay and total hospital costs in patients undergoing elective colorectal surgery were evaluated in this study.
Methods: Data from 90 consecutive patients undergoing elective colorectal resection between October 2006 and September 2009 was analyzed retrospectively. All patients received MBP. Patients in group A were given oral antibiotics (a total 480 mg of gentamycin, 4 gr of metronidazole in two divided doses and 2 mg of bisacodyl PO), whereas patients in group B received no oral antibiotics. Exclusion criteria were emergent operations, laparoscopic operations, preoperative chemoradiotherapy, intraoperative colonoscopy prior to the creation of an anastomosis or antibiotic use within the previous 10 days. SSI, length of hospital stays and total hospital charges were evaluated.
Results: Patients in both study groups, group A ($n = 45$) and group B ($n = 45$), were similar in terms of age, BMI, diverting ileostomy creation, localization and stage of the disease. Patients receiving oral antibiotics demonstrated a lower rate of wound infections (36% vs. 71%, $p < 0.001$), shorter hospital stay (8.1 ± 2.4 days vs. 14.2 ± 10.9 days, respectively, $p < 0.001$) and similar rates for anastomotic leakage (2% vs. 11%, $p = 0.20$). The mean ± SD total hospital charges were significantly lower in Group A (2.699 ± 0.892\$) than that in Group B (4.411 ± 4.995\$, $p = 0.029$).
Conclusion: Preoperative oral antibiotic use with MBP may provide faster recovery with less SSI and hospital charges.

1. Introduction

Surgical site infections (SSIs) increase the cost of care and are associated with increased morbidity and mortality and it is the

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third most common nosocomial infection, accounting for 14%–16% of all nosocomial infections among hospitalized patients [1]. Patients undergoing colorectal surgery are at risk for the development of SSIs, which may be up to 25% [2]. SSI surveillance has been shown to reduce SSI and various practices are used in an effort to decrease the relatively high rate of SSIs in patients who underwent colorectal resection [3]. While the prophylactic administration of IV antibiotics was reported to be advantageous, the value of mechanical bowel preparation (MBP) and prophylactic oral antibiotics is still debatable [4–7].

In this study, we aimed to evaluate the influence of oral antibiotic use together with MBP on surgical site infection (SSI) rate, length of hospital stay and total hospital costs in patients undergoing elective colorectal surgery.

2. Material and methods

The study protocol was approved by the institutional review board. Adult patients (>18 years old) who were admitted to the Department of Surgery at Ufuk University Hospital with colon cancer or ulcerative colitis between October 2006 and September 2009 were evaluated for the study. Patients giving written informed consent and appropriate for the study were included. Patients were assigned to one of the two groups consecutively, according to their order of admittance to the outpatient unit. Exclusion criteria were: emergent operations laparoscopic operations, preoperative chemoradiotherapy, intraoperative colonoscopy prior to creation of anastomosis or antibiotic use within the previous 10 days.

All patients received mechanical bowel preparation (MBP). Patients in the group A were given oral antibiotics (a total 480 mg of gentamycin, 4 gr of metronidazole in two divided doses and 2 mg of bisacodyl PO), while patients in the group B had no oral antibiotics.

Patients were admitted one day before surgery and received a cellulose-free liquid diet after admission. Parenteral hydration was started 8–12 h prior to the operation. MBP was performed by oral administration of 45 mL of sodium dibasic phosphate solution (Phosphosoda®, Fleet Pharmaceuticals, Lynchburg, USA) with water and a rectally applied Fleet enema (Phosphosoda®, Fleet Pharmaceuticals, Lynchburg, USA). Both groups received cefazolin 1 gr IV and metronidazole 500 mg IV during anesthesia induction, and these same medications were continued BID for five days postoperatively. In addition, patients in Group A received a total of 480 mg of gentamycin, 4 gr of metronidazole in two divided doses and 2 mg of bisacodyl PO. An overview of the preoperative MBP and antibiotic regimens are shown in Fig. 1.

All operations were performed by one of the two senior consultant surgeons. The surgical instrumentation, operating room facilities, and nursing teams were comparable for both groups. Total mesorectal excision for rectal cancer or mobilization of the splenic flexure for anterior resection was routinely used. The decision to suture or staple the colon was made by the senior surgeon at the time of operation. In general, anastomoses below the promontory were double stapled. Stapling included closing the distal remnant by TA or Roticulator® (AutoSuture, Covidien, USA) and joining the bowel ends using a Premium CEEA™ stapler (AutoSuture, Covidien, USA). If the anastomosis was performed by hand, single inverted continuous sutures followed by a second layer of single interrupted sutures were placed. The abdominal cavity was irrigated with 2 liters of warm saline before closure. The abdominal wall was approximated with a continuous 1-0 PDS suture, and then the skin was closed with interrupted 3-0 polypropylene sutures.

A structured log was kept to record any signs or treatment of infection for each patient by the same independent surgeon throughout the whole 30-day postoperative follow-up period, who did not have any influence in the clinical management of the patients. SSI were classified as being either incisional or organ/space. Incisional SSIs were further divided into those involving only skin and subcutaneous tissue (superficial incisional SSI) and those involving deeper soft tissue of the incision (deep incisional SSI). Organ/space SSIs involve any part of anatomy other than incised body wall layers that was opened or manipulated during operation. The SSI criteria based on the description of Horan TC are shown in Table 1 [8]. In addition to this, Clavien/Dindo categorization was also used in the classification of morbidity of the patients in postoperative period [9]. Anastomotic dehiscence was diagnosed clinically and confirmed radiologically or during corrective surgery. Each patient was followed for 30 days post-operatively through weekly clinic visits where wounds were assessed for infection and anastomotic failure.

Length of stay in the hospital was calculated as the period from the day of surgery until discharge. Hospital death was defined as mortality from any cause within 30 days of hospitalization. Hospital charges were calculated as the sum of charges for daily hospital stay (bed fee), medications and medical supplies.

3. Statistical analysis

Data analyses were performed with SPSS for Windows, version 11.5 (SPSS Inc., Chicago, USA). Age, duration of operation, day of first defecation and length of hospitalization were expressed as mean ± SD. Mean ages were compared by unpaired t testing. Otherwise, the Mann-Whitney *U* test was used to compare the duration of operation, stage of tumor, time to first defecation and length of hospitalization. Categorical data were analyzed by Fisher's exact test and χ^2 test, where applicable. A p value less than 0.05 was considered statistically significant. Based on a pilot study and clinical experience, a total sample of at least 86 cases (43 for preoperative oral antibiotic, 43 for no preoperative oral antibiotic) was required to detect at least a 4-day difference in length of stay and 30% difference in wound infection rates with a power of 85% at the 5% significance level.

4. Results

During the study period, 121 patients with lesions necessitating colorectal resection presented to our surgical clinic. Of these, 90 patients (45 in Group A and 45 in Group B) with colorectal cancer (n = 85) and ulcerative colitis (n = 5) agreed to participate and were suitable for the study. Group A patients were 27 males and 18 females with a mean age of 58 ± 17 years (range 19–85 years) and Group B patients were 27 males and 18 females with a mean age of 59 ± 12 years (range 28–87 years). The groups did not differ with regard to age, gender ratio, or the presence of any concomitant disease (Table 2).

Table 3 shows the operative details of the patients in both groups. Groups A and B did not differ regarding the stage or site of tumors, the rectosigmoidal junction being the most common localization for both groups. Both groups were also similar in regard to operational procedure, stapler usage, and rate of preoperative or postoperative blood transfusion. Operative time in Group A (146 ± 41 min, range 75–240 min) was lower than that of Group B (166 ± 39 min, range 75–300 min, p = 0.012).

Table 4 shows the operative and clinical outcomes of both groups. The morbidity rate that was calculated according to the Clavien/Dindo definition was 26% (12 patients) in Group A. Four of these 12 patients were classified as Grade 1 (33%), 2 patients as Grade 2 (16%), 3 patients as Grade 3a (2%) and 1 patient as Grade 3b (8%). Morbidity rate was 37% in Group B which consisted of 17

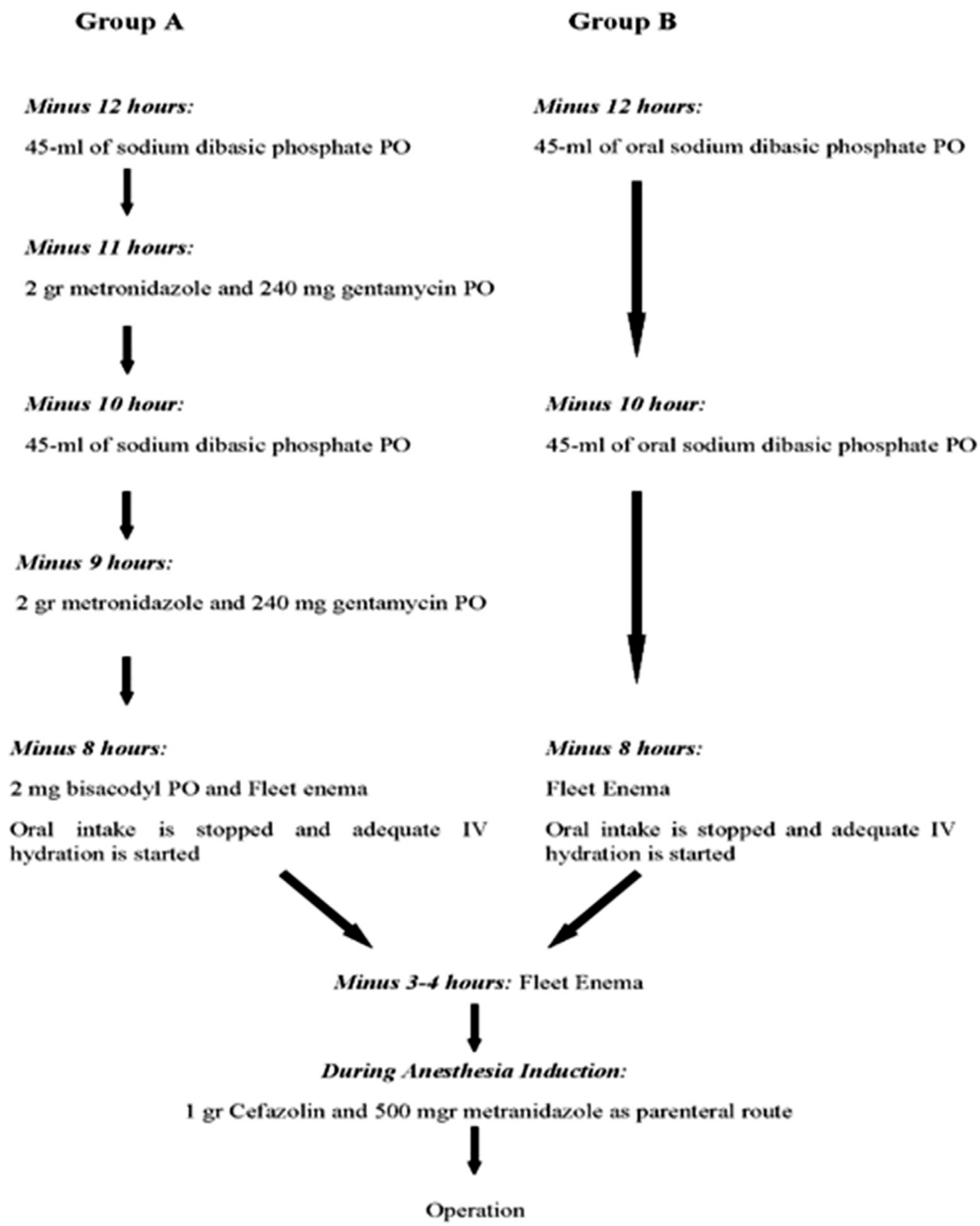

Fig. 1. Preoperative preparation protocols of two groups.

patients, 4 of which were in Grade 1 (44%), 5 patients in Grade 2 (29%), 1 patient in Grade 3a, 6 patient in Grade 3b (35%) and 1 patient in Grade 4a (5%).

SSIs were diagnosed in 16 patients in group A (35%) and 32 patients in group B (71%). The differences in SSI rates between the groups were statistically significant ($p < 0.001$). The rates of anastomotic leakage were 2% and 11% in Group A and B respectively, and this difference did not reach statistical significance ($p = 0.203$).

In Group A, superficial SSIs were noted in 11 patients. Superficial incisional SSI was reported in 9 patients. Redness ($n = 6$), swelling ($n = 6$) and heat ($n = 4$) were the major findings for the diagnosis of superficial SSIs. Deep SSI was reported in 2 patients. Purulent drainage was the major finding in these patients and they underwent deliberately opened incision. Culture antibiograms were found to be negative in these patients subsequently. The organ/space SSIs were reported in 2 patients that were diagnosed by a purulent drainage in 1 patient and evidence of abscess that was detected by clinical examination and confirmed radiologically. One of them was managed with percutaneous drainage and the other by repeating laparotomy. Culture antibiogram was positive in only one of these patients where *Escherichia coli* and *Klebsiella pneumoniae* was detected.

In Group B, 32 patients had superficial SSI. Twenty-one of these had superficial incisional SSI; nine of them were presented with redness, 11 with swelling, 8 patients with heat and 1 of them with purulent drainage. Deep Incisional SSI was reported in four patients whose symptoms were fever greater than 38 °C in 1 patient, purulent drainage, localized pain and tenderness in 2 patients and spontaneous dehiscence in 1 patient. *Staphylococcus aureus* and *Klebsiella pneumoniae* growth were detected in two out of three culture antibiograms. The organ/space SSIs were detected in 7 patients by purulent drainage and by radiological evidence of infection in 2 patients, and during reoperation in 5 patients. They were managed with percutaneous drainage in one patient and

Table 1
Criteria of SSI based on Horan TC description.

Criteria for defining a surgical site infection (SSI)	
Superficial Incisional SSI Infection occurs within 30 days after operation and infection involves only skin or subcutaneous tissue of the incision and at least one of the following:	i. Purulent drainage, with or without laboratory confirmation, from the superficial incision. ii. Organisms isolated from an aseptically obtained culture of fluid or tissue from the superficial incision. iii. At least one of the following signs or symptoms of infection: pain or tenderness, localized swelling, redness, or heat and superficial incision iv. Diagnosis of superficial incisional SSI by the surgeon or attending physician.
Deep Incisional SSI Infection occurs within 30 days after the operation if no implant[a] is left in place or within 1 year if implant is in place and the infection appears to be related to the operation and infection involves deep soft tissues (e.g., fascial and muscle layers) of the incision and at least one of the following:	i. Purulent drainage from the deep incision but not from the organ/space component of the surgical site ii. A deep incision spontaneously dehisces or is deliberately opened by a surgeon when the patient has at least one of the following signs or symptoms: fever (>38 °C), localized pain, or tenderness, unless site is culture-negative iii. An abscess or other evidence of infection involving the deep incision is found on direct examination, during reoperation, or by histopathologic or radiologic examination. iv. Diagnosis of a deep incisional SSI by a surgeon or attending physician.
Organ/Space SSI Infection occurs within 30 days after the operation if no implant[a] is left in place or within 1 year if implant is in place and the infection appears to be related to the operation and infection involves any part of the anatomy (e.g., organs or spaces), other than the incision, which was opened or manipulated during an operation and at least one of the following:	i. Purulent drainage from a drain that is placed through a stab wound[b] into the organ/space. ii. Organisms isolated from an aseptically obtained culture of fluid or tissue in the organ/space. iii. An abscess or other evidence of infection involving the organ/space that is found on direct examination, during reoperation, or by histopathologic or radiologic examination. iv. Diagnosis of an organ/space SSI by a surgeon or attending physician.

[a] National Nosocomial Infection Surveillance definition: a nonhuman-derived implantable foreign body (e.g., prosthetic heart valve, nonhuman vascular graft, mechanical heart, or hip prosthesis) that is permanently placed in a patient during surgery.
[b] If the area around a stab wound becomes infected, it is not an SSI. It is considered a skin or soft tissue infection, depending on its depth.
Adapted from Horan TC et al. CDC definitions of nosocomial surgical site infections, 1992: a modification of CDC definitions of surgical wound infections [8].

Table 2
Demographic characteristics and concomitant diseases of patients undergoing elective colorectal resection. Group A (n = 45) received prophylactic oral antibiotics several hours before surgery, Group B (n = 45) received no oral antibiotics.

Variables	Group A	Group B	p
Sex (F/M)	18/27	18/27	1.00
Age [years]	58 ± 17 [19–85]	59 ± 12 [28–87]	0.801
Concomitant diseases	27 (60%)	28 (62%)	0.985
Diabetes mellitus	11 (24.4%)	10 (22.2%)	
Atherosclerotic vascular disease	5 (11.1%)	6 (13.3%)	
Hypertension	9 (20.0%)	9 (20.0%)	
Pulmonary disease	2 (4.4%)	3 (6.7%)	

Table 3
Operative procedures performed, tumor stage, and incidence of blood transfusions in patients undergoing elective colorectal resection. Group A (n = 45) received prophylactic oral antibiotics several hours before surgery, Group B (n = 45) received no oral antibiotics. The differences that reach statistical significance are denoted in **bold**.

Variables	Group A	Group B	P
Operative procedure	45	45	0.400
Right hemicolectomy	9 (20.0%)	8 (17.8%)	
Left hemicolectomy	5 (11.1%)	5 (11.1%)	
Transverse colectomy	2 (4.4%)	7 (15.6%)	
Low anterior resection	23 (51.1%)	22 (48.9%)	
Total colectomy	6 (13.3%)	2 (6.7%)	
Diverting ileostomy	21 (46.7%)	14 (31.1%)	0.195
Duration of operation (minutes)	146 ± 41 (75–240)	166 ± 39 (75–300)	**0.012**
Tumor stage (A/B/C/D)	1/17/27/0	3/10/29/3	0.211
Preoperative blood transfusion	12 (26.7%)	15 (33.3%)	0.645
Postoperative blood transfusion	32 (71.1%)	35 (77.8%)	0.629

Table 4
Operative outcomes, length of hospital stay, and total hospital charges of patients undergoing elective colorectal resection. Group A (n = 45) received prophylactic oral antibiotics several hours before surgery, Group B (n = 45) received no oral antibiotics. The differences that reach statistical significance are denoted in **bold**.

Variables	Group A	Group B	p
Anastomotic dehiscence	1 (2.2%)	5 (11.1%)	0.203
Wound infection	16 (35.6%)	32 (71.1%)	**<0.001**
Length of stay (days)	8.1 ± 2.4 (5–16)	14.2 ± 10.9 (4–50)	**<0.001**
Total hospital charges [$]	2699 ± 0,892	4411 ± 4995	**0.029**

relaparotomy in the remaining 6 patients. Culture antibiograms were negative in 3 patients and positive in the other three (*Escherichia coli* in two patients and *Klebsiella pneumoniae* in one patient). Diverting ileostomy was performed in 5 patients due to anastomotic dehiscence.

In patients who did not develop a wound infection, the length of stay was similar between the two groups: 7.5 ± 2.1 days (range, 5–15 days) for Group A and 7.8 ± 2.2 days (range 4–13 days) for Group B (p = 0.648). But, older age was related to a higher incidence of wound infections: the mean age of the patients who developed wound infections was 62 ± 12 years (range 23–85 years), whereas the mean age of those who did not develop wound infections was 56 ± 16 years (range 19–87 years) (p = 0.057). Antibiotic-associated pseudomembranous colitis, bacterial superinfection or bacterial resistance did not develop in any of the study patients.

Length of stay was shorter in Group A [mean 8.1 ± 2.4 (range 5–16) days], than that in Group B [mean 14.2 ± 10.9 (range 4–50) days, p < 0.001)]. The mean ± SD total hospital charges were lower in Group A (2699 ± 0,892 $) compared to Group B (4411 ± 4995$, $p = 0.029$).

5. Discussion

For many years, surgeons believed that postoperative peri-anastomotic sepsis was due to contamination during surgery. In the 1920s, the great surgeon Andrew Moynihan was the first to describe sepsis resulting from anastomotic leakage [10]. Since then, many factors have been found to be associated with a higher risk of SSI in these patients: male gender, older age, obesity, cigarette smoking, inappropriate preoperative IV prophylactic antibiotics, perioperative blood transfusion, intraoperative hypothermia (≤36 °C), poor glycemic control in diabetic patients (>200 mg/dL), site of anastomosis, technical details related to operation such as blood supply and tension at the anastomotic line, operative time of greater than 215 min, preoperative peritoneal sepsis, stoma, fecal soiling, and greater fecal load [11–17]. Improvements in intraoperative thermal regulation and perioperative glycemic control are examples of other techniques that can reduce the rate of SSI [11,18].

SSIs can be prevented with the administration of proper antibiotics up to 60% [18]. Long-term antibiotics (e.g. five days, as it was used in this study) have also been used as prophylaxis against postoperative wound infections [6,19,20]. Regarding administration of perioperative prophylactic antibiotics to colorectal resection patients, some authors found no benefit of oral antibiotics [6,7]. However, the addition of oral antibiotics to mechanical bowel preparation was reported to cause a significant decrease in SSI in colon resections by some others (8.6% vs. 19.5%) [21,22]. But the same result was not confirmed for patients undergoing rectal resection [21]. Of note, the use of prolonged IV antibiotics did not cause any superinfection or C. difficile infection in this study. Our findings support clinical benefit of prophylactic oral antibiotics in both colon and rectum resection.

Our SSI rates were among the highest in the literature. This may be due to both our methods and our patients: data was collected prospectively in a detailed fashion according to CDC criteria by a single surgeon and infection control nurse, up to 30 days postoperatively [8]. Almost half of our patients underwent rectal surgery, which is known to have a higher rate of wound infection than that in colon surgery [21]. The wide variation in SSI rates after colorectal surgery reported in the literature may be due to methodological issues (e.g. different diagnostic criteria, observer bias, and the duration of follow-up) [23]. For example, some authors defined wound infection as a wound with drainage of a purulent collection, which required partial or complete opening, or erythema requiring initiation of an antibiotic treatment [24]. Similarly in this study, the appearance of any sign of wound infection, such as pain, erythema, tenderness, induration, odor, purulent drainage and heat on the insicion site that was developed within 30 days postoperatively was recorded as SSI even in the absence of positive cultures. A number of factors were demonstrated to associate with culture negative SSIs, including the type of the microorganism, the source of the sample, patient related conditions, previous antibiotic use, and laboratory-dependent issues such as the duration and type of the media used to detect the microorganism. Moreover in several studies, approximately half of SSIs occurred after the patient left the hospital, and thus may be missed if follow-up was lax [25–28]. Many studies were retrospective in design, thus their accuracy in reporting the presence or absence of wound infection may be questionable. Careful documentation and a longer follow-up period in our study might have resulted in our relatively high rate of SSIs.

The incidence of anastomotic leakage in patients undergoing MBP was reported to be 0%–9.7% [20,29–35]. Moreover, lower rectal anastomoses have been shown to have a higher risk of leakage [36]. Although half of the patients in each group underwent low anterior resection with a lower rectal anastomosis, the rate of anastomotic dehiscence in patients who received preoperative oral antibiotics (Group A) was only 2%. This result is much better than that of most other series. However, if oral antibiotics were not included as part of the preoperative bowel preparation (Group B), the anastomotic dehiscence rate increased up to 11%.

Studies with large patient populations reporting outcomes after colorectal resection abound in the literature [24,30,33,37]. Although variables regarding operative techniques and equipment were similar in both of our patient groups, operation time differed by only 20 min, and the mean operative time for both groups was well below the 215 min threshold (for increased risk of infection) reported in the literature [14]. In the present study, adequate fluid and electrolyte replacement was started 8–12 h before surgery, and no major problems related to fluid or electrolyte imbalance occurred. Maintenance of normothermia, prevention of hypoglycemia and the timing of the beginning of oral supplementation were achieved by the same nursing team for the two groups of patients. In our study, we found that oral antibiotics caused a decrease in SSI and the pathogen microorganisms were similar in both groups. This can be explained by the fact that oral antibiotics decrease the amount of bacteria found in the colon, which in turn, decreases the risk of SSI. Although some authors proposed that preoperative antibiotics might result in bacterial superinfection or resistance, we did not observe any adverse effects related to the pre-operative use of oral antibiotics in our patients.

A recent review by Zelhart et al. clearly summarized the historical evolution of bowel preparation in patients undergoing colorectal surgery [38]. Although the best regiment for bowel preparation is yet inconclusive, the use of preoperative prophylactic antibiotics is strongly recommended in almost all current guidelines [38–41]. Similarly, there is strong evidence in favor of the use of preoperative oral antibiotics. However, whether preoperative oral neomicin and erythromycine/metronidazole treatment is effective only in the settings of mechanical bowel preparation remains elusive [38,42]. Herein, we suggest that the use of preoperative oral antibiotics together with parenteral antibiotics and mechanical bowel preparation is effective against the development of SSIs in patients undergoing colorectal surgery. Yet, more prospective randomized studies with larger sample size are required in the decision for the best preparatory regimen in patients in whom colorectal surgery is planned.

6. Conclusion

Two doses of oral gentamycin and metronidazole given a few hours preoperatively to elective colorectal resection patients, in addition to mechanical bowel preparation, reduced wound infection, length of hospital stay and total hospital charges. To test our results in a more robust fashion, randomized, blinded studies to compare mechanical bowel preparation with and without prophylactic oral antibiotics should be performed in patients who are about to undergo colorectal resection.

Ethical approval

The study protocol was approved by the Ufuk University Institutional Review Board.

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Author contribution

Suleyman Ozdemir-study design, patient recruitment, principal surgeon, data collection, data analysis, writing, editing.

Kamil Gulpinar-study design, patient recruitment, attending surgeon, data collection, writing, editing.

S. Erpulat Ozis-study design, patient recruitment, attending surgeon, data collection, writing, editing.

Zafer Sahli-study design, patient recruitment, attending surgeon, data collection, data analysis, writing, editing.

S. Altug Kesikli-data collection, data analysis, writing, editing.

Atila Korkmaz-study design, patient recruitment, senior surgeon, writing, editing.

I. Ethem Gecim-study design, patient recruitment, senior surgeon, writing, editing.

Conflict of interest statement

None.

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