Systemic use of antibiotics does not prevent postoperative infection in elective colorectal surgery: a randomized controlled trial

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Abstract We assessed the clinical impact of the systemic use of antibiotics on postoperative infection in colorectal surgery. Perioperative administration prevents postoperative infection: a statement which is based on the results of five randomized controlled trials performed in the 1970s and 1980s. Our study design was a randomized controlled trial. We created two groups, one using the systemic antibiotic cefotiam (CTM), and the other using no antibiotic as the control. The primary end point was the overall postoperative infection rate. There were 100 patients assigned to this study. The patients were divided into two groups; the control group consisted of 51 cases and the CTM group had 49 cases. The backgrounds of the patients in the two groups were not significantly different. The overall postoperative infection rate was 28/51 (54.9%) in the control group and 25/49 (51.0%) in the CTM group. The surgical site infection (SSIs) (superficial, deep, and space/organ) were 23/51 (45.1%) in the control group and 20/49 (40.8%) in the CTM group. No significant difference was observed between the CTM group and the control group regarding postoperative infection after elective colorectal surgery.

Key words Colorectal surgery · Postoperative infection · Systemic use · Antibiotic · Randomized controlled trial · Prophylaxis

Introduction

An antimicrobial agent must be administered at the location of an infection. However, if prophylactic antibiotics are administered to the locus where no infection exists, will they prevent infection? In order to address this question, we must reconsider the administration of antibiotics that are used to prevent postoperative infection. The conclusion that “perioperative administration prevents postoperative infection” was based on the results of five randomized controlled trials performed in the 1970s and 1980s. However, both the antimicrobial agents and postoperative care have changed greatly in the past 30 years. As a result, we decided to investigate whether the “perioperative administration of antibiotics can prevent postoperative infection” at the present day. Regarding the use of second-generation cephalosporin (cefotiam, CTM) as a prophylaxis of colorectal postoperative infection, we followed both the Japanese and the US guidelines.6,7

Methods

The study design was a randomized controlled trial, which began in July 2002. Colorectal surgery was about to be performed for each patient, and informed consent had been obtained in writing from the patients preoperatively. We divided the patients into two groups, one of which received systemic antibiotics, while the other received no antibiotics and thus was used as a control. The study was carried out in two hospitals that were both affiliated to the Nihon University School of Medicine. The study was registered as a randomized controlled trial with university hospital medical information network (UMIN). The registration number was 000000870, and the study was entitled “The evaluation of a systemic antibiotic effect for colorectal surgery.” The trial received the approval of the Ethics Committee. All the patients who had the operation had been diagnosed with colon cancer. This was a criterion for choice, and all other patients were excluded from the study. The subjects were any man or woman who had undergone either an open colectomy or a laparoscopic colectomy between the ages of 16 and 79 years.

The following groups were automatically excluded from the study.

1. Those who had had a total colectomy, a dirty or contaminated operation, an operation for a perforation, or an emergency operation.
2. Those who were 15 years old or younger, and those who were 80 years old or older.
3. Patients with serious complications (e.g., heart, lung, liver, kidney dysfunction, diabetes, a tendency to hemorrhage, etc.).
4. Patients with a preoperative infection.
5. Patients who had undergone long-term administration of adrenocortical hormones.

Duration and alterations of randomized controlled trials
1. We checked for signs of infection (fever, white blood cell count, and C-reactive protein), and if the patient had no infection we did not administer any antibiotics to either group after the 4th postoperative day.
2. If the patient had an infection, we administered the appropriate antibiotics to the patient at that time.

Sepsis followed the definition of systemic inflammatory response syndrome (SIRS), and SSI was assessed by the definition of the National Nosocomial Infections Surveillance (NNIS) system. We determined the presence of antibiotics by consulting the patient’s family doctor.

We checked laboratory and chest X-ray results between the 3rd and 7th postoperative days, and examined a patient at any time it was deemed necessary.

The criteria of postoperative infection were as follows:
1. Fever: over 38.0°C;
2. White blood cell count: over 12,000/μl or less than 4000/μl;
3. C-reactive protein: over 10 mg/dl.

We started antibiotics in cases of infection that satisfied two or more of the conditions mentioned above. The final judgment occurred between the 10th and 14th postoperative days or at discharge.

Administrative procedures
In the antibiotic group, CTM was administered with a drip infusion before the skin incision. In cases where a long operation was needed, CTM was added every 3 h. From the 1st to the 3rd postoperative day, 1 g CTM was administered every morning and evening. In the control group, no antibiotic was administered. All patients agreed to this study arrangement, and approval was received from the Ethics Committee.

Entry and stratification
The sample size was set at 100 cases because the postoperative infection rate is normally expected to be around 20% when prophylactic antibiotics are used. Preoperatively, the patients were grouped according to the type of surgery (i.e., the colon or the rectum), according to age (i.e., either 60 years or older, or below 60 years), and those with a preoperative total protein volume of 6.5 g/dl or less.

Surveillance system
The surveillance data recorded were age, sex, diagnosis, total preoperative protein, American Society of Anesthesiologists (ASA) classification, date of operation, operative procedure, colostomy/closure, operating time, hemorrhage, transfusion, type of postoperative infection, and date of outbreak.

Prophylaxis procedures before, during, and after the operation
The following procedures were carried out routinely for all patients.

Before the operation. A 500-ml saline enema 2 days before the operation, fasting and a laxative 1 day before the operation, and a glycerin enema on the day of the operation. Standard mechanical preparations were enforced for all patients.

During the operation. Employment of a wound protector, absorbable string against muscle fascia, peritoneum sutures, and suction drainage. Change of surgical globe. The intra-abdominal cavity was washed at the end of the operation. Use of a double-stapling technique for auto-sutures, and povidone–iodine sterilization for the anal side of the anastomotic region in a low anterior resection.

After the operation. Employment of a hydrocolloid dressing and no wound sterilization. The nasogastric tube was pulled out on the 1st or 2nd postoperative day.

Statistical analysis
The clinical and surgical data were compared between the two groups using the t-test/Fisher’s extra test. P values of < 0.05 were considered to be statistically significant. An analysis was carried out on an intention-to-treat basis using the statistical package for social science. The effect of prophylactic antibiotics on primary outcomes was tested using a two-tailed Pearson χ² test.

Results
One hundred patients were assigned to this study from July 2002 to January 2007. Seven patients could not be included, but were analyzed by the rules of intention to treat, and the patients were divided into two groups. The control group consisted of 51 cases and the CTM group had 49 cases (Fig. 1). Of these cases, 56 were men and 44 were women. There were no differences in age, preoperative total protein, or number of preoperative oral anticancer agents between the two groups (Table 1). The operative procedures were partial colectomy in 26 cases, low anterior resection in 14 cases, and abdominoperineal resection in 5 cases in the control