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Original Article

Antimicrobial Prophylaxis and Colon Preparation for Colorectal Surgery: Results of a Questionnaire Survey of 721 Certified Institutions in Japan

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Abstract

Purpose. Antimicrobial prophylaxis (AMP) can reduce the risk of surgical site infection (SSI) in gastroenterological surgery; however, in Japan its use was not fully recognized before 2000. The first nationwide guideline was published in 2001, since when the use of AMP has improved gradually. We conducted this study to investigate the current implementation of AMP in colorectal surgery and adherence to recommended practices for preventing SSI in Japan.

Methods. A questionnaire survey was sent to hospitals accredited by the Japanese Society of Gastroenterological Surgery and the Japan Society for Surgical Infection (JSSI). The questionnaire focused on the AMP regimen used for colorectal surgery.

Results. Responses were received from 721 (58%) of the 1249 hospitals that were sent the survey. The initial AMP dose was administered within 1 h before incision at 94% of the responding institutions. AMP was discontinued within 24 h of surgery at only 10% of institutions. Second-generation cephalosporins were administered at 84% of the institutions.

Conclusions. The appropriate use of AMP in colorectal surgery is incomplete in certified institutions in Japan. The fact that many institutions administer AMP for longer than recommended is a problem that needs to be addressed.

Key words Surgical site infection · Colorectal surgery · Questionnaire

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Introduction

Surgical site infection (SSI) is the most frequent nosocomial infection in surgical patients, and accounts for 38% of all such infections.[1,2] Surgical site infection prolongs hospital stay, increases medical costs, and occasionally leads to mortality.[1,3,4] The United States Centers for Disease Control and Prevention (CDC) guidelines for the prevention of SSI are accepted widely in Japan, and various perioperative procedures have been changed and made more effective in accordance with these guidelines. We reported previously that the introduction of various perioperative procedures helped reduce the incidence of SSI.[5] Furthermore, the Centers for Medicare and Medicaid Services and CDC implemented the Surgical Infection Prevention (SIP) Project, and an overview of the Surgical Care Improvement Project (SCIP).[6] The aim of the project, which is widely known in Japan, is to decrease the morbidity and mortality associated with postoperative SSI by promoting appropriate selection and timing of the administration of antimicrobials prophylaxis (AMP).

In Japan, the appropriate use of AMP was not fully recognized until 2000, and the first nationwide guideline was published in 2001. The use of AMP has subsequently improved over the last decade. However, in their 2003 study of patients undergoing digestive tract surgery, Sumiyama et al.[7] reported that 28% of patients in Japan did not receive AMP before surgery. Moreover, only 3% of the responding institutions discontinued prophylactic antimicrobial agents within 24 h after surgery and 18% of the responding institutions gave preoperative oral antibiotics. The aim of the present survey conducted by the Committee for Quality and Safety in Healthcare, part of the Japan Society for Surgical Infection (JSSI), was to investigate the current implementation of AMP

in colorectal surgery and adherence to the recommended practices for preventing SSI in Japan.

Materials and Methods

In September 2008, a questionnaire survey was sent to 1249 hospitals accredited by the Japanese Society of Gastroenterological Surgery and the JSSI. This questionnaire surveyed the use of AMP and preoperative colon preparation for colorectal surgery, including the following: the time of the first dose of antimicrobial therapy; the duration of AMP; the dosing regimen; the agents used; mechanical bowel preparation; and the oral administration of nonabsorbable antimicrobial agents (Table 1).

This survey included open and laparoscopic surgery, and was sent to senior colorectal surgeons. The responses were returned by mail. On receipt of the completed questionnaires, data were recorded anonymously and analyzed in an electronic database. Data were reported as numbers and proportions of submitted answers. As not all questionnaires were filled in completely, the denominator may vary between different items. The total number of responses for each question is reported for each item.

Results

We received responses from 721 of the 1249 hospitals surveyed: a response rate of 57.7%. Table 2 summarizes

Table 1. Questionnaire survey

When is the first dose of antimicrobial therapy administered?	More than 1 h before incision
	Within 1 h before incision
	After incision
Duration of antimicrobial prophylaxis	12 h after completing surgery
	12–24 h
	24–48 h
	48–72 h
	72–96 h
	More than 96 h
Antimicrobial dosing interval	Every 12 h
	Every 8 h
	Other
Antimicrobial prophylaxis agent used	First-generation cephalosporin
	CMZ/FMOX
	CTM
	Third-generation cephalosporin
	Fourth-generation Cephalosporin
	SBT/CPZ
	SBT/ABPC
	TAZ/PIPC
	Cephalosporin+clindamycin
	Fluoroquinolones
	Others
Preoperative timing of oral nonabsorbable antibiotics	More than 2 days before the operation
	One day before the operation
	No use
Oral antimicrobial agents used	Kanamycin
	Polymyxin B
	Erythromycin
	Metronidazole
	Fluoroquinolones
	Cephalosporins or penicillins
	Others
Approach for preoperative mechanical bowel preparation	Polyethylene glycol
	Sodium phosphate
	Others
	Mechanical bowel preparation not performed

CMZ, cefmetazole (second-generation cephalosporin [cephamycin]); FMOX, flomoxef (second-generation cephalosporin [oxacephems]); CTM, cefotiam (second-generation cephalosporin without anaerobic activity); SBT/CPZ, sulbactam–cefoperazon sodium; SBT/ABPC, sulbactam–ampicillin sodium; TAZ/PIPC, piperacillin–tazobactam

the general characteristics of responding hospitals. There were 390 public hospitals (54.1%). The Diagnosis Procedure Combination (DPC) payment system, a modification of the Diagnosis Related Grouping Prospective Payment System (DRG-PPS) of the United States, was used in 52.7% of responding hospitals. About 40% of the responding hospitals had 200–399 beds.

Timing of the First Dose of Antimicrobial Therapy

Overall, 714 institutions (99% of the responding institutions) answered this question. The relationship between antimicrobial start time and first incision is shown in Fig. 1. The first antimicrobial dose was administered within 1 h before incision in 668 institutions (93.6%).

Table 2. General characteristics of the responding hospitals

Characteristic	No. of hospitals
University hospitals, *n* (%)	111 (15.4%)
Ownership, *n* (%)	
Public	390 (54.1%)
Private	186 (25.8%)
Other	34 (4.7%)
Payment system, *n* (%)	
DPC	380 (52.7%)
Japan's fee-for-service	341 (47.3%)
Number of beds, *n* (%)	
<200	106 (14.7%)
200–399	289 (40.1%)
400–599	161 (22.3%)
600–799	95 (13.2%)
>800	64 (8.9%)
Other	6 (0.8%)

DPC, Diagnosis Procedure Combination

Duration of AMP

A total of 712 institutions (99% of the responding institutions) answered the question on the duration of AMP in colorectal surgery. The proportion of institutions in which the prophylaxis was discontinued within 24 h after surgery is shown in Fig. 2. Only institutions 74 (10.4%) discontinued prophylactic antimicrobial agents within 24 h. In almost half of the institutions, AMP was continued for 48–72 h.

AMP Dosing Interval

In 595 of the 638 institutions in which AMP was administered for more than 24 h, the dosing interval was every 12 h. Only 43 institutions (6.7%) administered AMP every 8 h.

Selection of Agents

A total of 720 institutions (99% of the responding institutions) answered this question. Some of the responding institutions reported that they used more than one agent. In total, 845 agents were reported for use in colon surgery and 849 agents were reported for use in rectal surgery. Second-generation cephalosporins were used in 84% of the institutions. Cefotiam, a second-generation cephalosporin without activity against anaerobic bacteria, was used in about 20% of the institutions (Fig. 3). Because intravenous metronidazole was not available in Japan, the combination of cefazolin and metronidazole was not used in any of the hospitals.

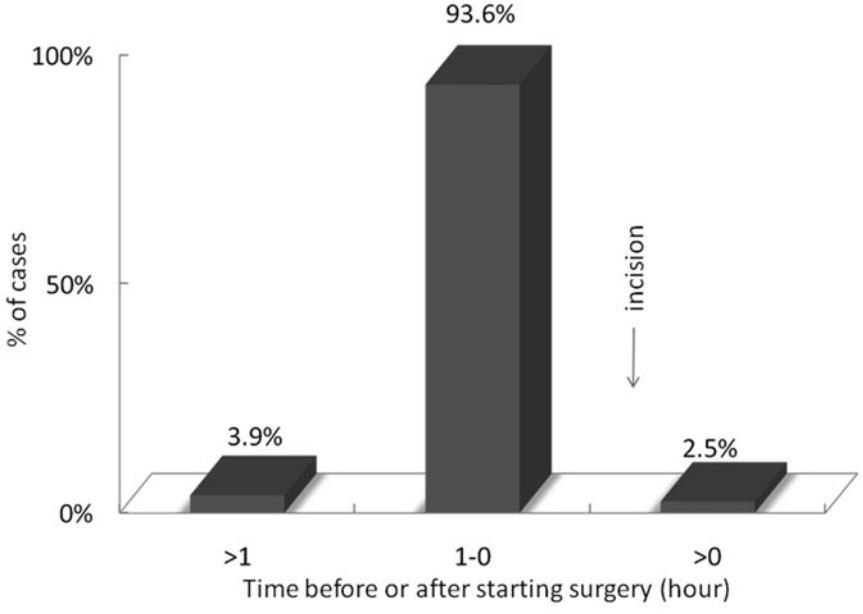

Fig. 1. Timing of the first dose of antimicrobial therapy in colorectal surgery

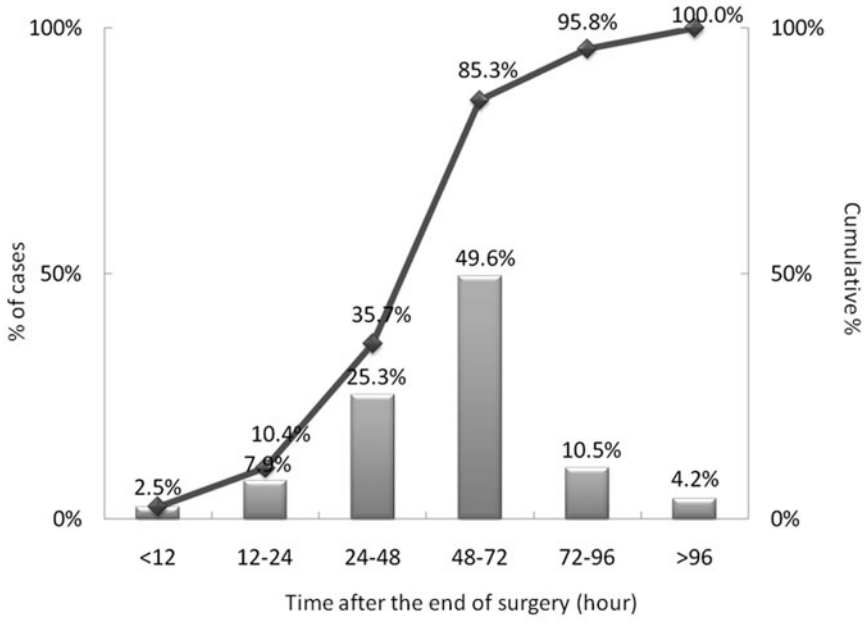

Fig. 2. Time to discontinuation of antimicrobial prophylaxis in colorectal surgery *Bars* show the proportion of hospitals that discontinued antimicrobial prophylaxis at each time interval. *Line* shows the cumulative proportion of hospitals in which antimicrobial therapy was discontinued

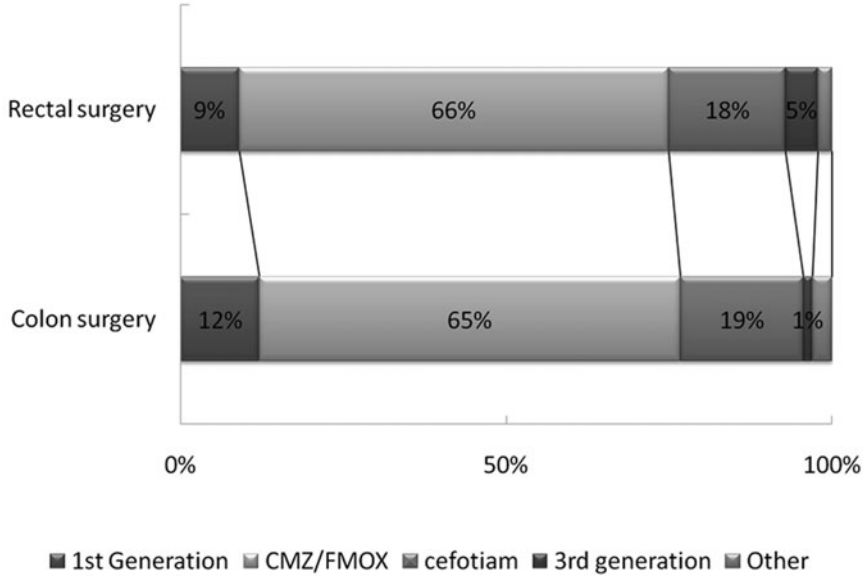

Fig. 3. Type of antibiotics administered for colorectal surgery. *CMZ*, cefmetazole (second-generation cephalosporin [cephamycin]); *FMOX*, flomoxef (second-generation cephalosporin [oxacephems]); cefotiam (second-generation cephalosporin without anaerobic activity)

Mechanical Bowel Preparation

Overall, 713 of the 721 institutions answered the question regarding preoperative mechanical bowel preparation. Mechanical bowel preparation was performed preoperatively at 705 institutions; as polyethylene glycol at 339 institutions; sodium phosphate at 256 institutions; and others at 110 institutions. Only eight institutions (1.1%) did not use mechanical bowel preparation.

Oral Administration of Nonabsorbable Antimicrobial Agents

A total of 714 institutions (99% of the responding institutions) answered this question. Oral antibiotics were rarely given, with only 84 institutions (11.7%) reporting their use. Only 34 of these 84 institutions (40.5%) selected a regimen that covered both anaerobic and aerobic organisms (Table 3).

Adherence to Clinical Guidelines

Table 4 shows the adherence to the CDC guidelines for antimicrobial use to prevent SSI after colorectal surgery. The use of AMP in colorectal surgery in accordance with the guidelines was only partially compliant in the certified institutions in Japan. Many institutions administered AMP for longer than recommended. Although a worldwide consensus for preoperative colon prepara-

tion has not been reached, the usefulness of oral AMP is not underlined in Japan.

Discussion

This survey gives an overview of the current use of prophylactic antimicrobials in colorectal surgery in Japan. This kind of surveillance reflects better results than the actual nationwide standard, as the hospitals that returned the questionnaires have academic interest in SSI issues. The CDC and current clinical guidelines recommend dosing within 1 h before the first incision.[1,6] In randomized clinical trials, antimicrobial agents given before, during, and shortly after abdominal surgery were effective in preventing SSI.[8,9] Stone et al. reported that the lowest rates of SSI after abdominal operations were associated with prophylaxis started within 1 h before the first incision.[10] In 1993, Sumiyama et al. reported that only 19.3% of the responding institutions in Japan gave antibiotics to all patients during surgery, including immediately before and during surgery.[11] The responses to a later questionnaire in 2003 revealed that this rate had increased to 70%.[7] In the present survey, 93.6% of the responding institutions administered prophylactic antimicrobial agents within 1 h before the first incision. In a United States survey, Bratzler et al. reported that an antimicrobial dose was administered within h before incision to 55.7% of patients in 2001, and to 69.7% of patients in 2004.[12] This suggests that the timing of the first dose of antimicrobial therapy regimen is consistent with the current guidelines in Japan.

Maintaining therapeutic antibiotic levels in the serum and tissues throughout the operation until, at most, a few hours after surgery reduces the risk of SSI.[1] In Western countries, short-term AMP is recommended for all gastrointestinal operations, although the optimal duration of prophylaxis is controversial. Many surgeons continue giving antimicrobials for 2–3 days after the operation based on the rationale that surgical drains and intravenous catheters might lead to bacterial seeding of the surgical site.[13] However, this needs to be balanced against the development of resistant strains if AMP is prolonged. Bratzler et al. reported that AMP was discontinued within 24 h after completing surgery for 40.7% of the patients in 2001.[13] In a later report, antimicrobial therapy was discontinued within 24 h after surgery in 52.9% of patients who received treatment in the fourth quarter of 2004.[12] In the present survey, only 10.4% of the responding institutions discontinued AMP within 24 h of surgery. However, the duration of postoperative antimicrobial prophylactic administration has decreased steadily in Japan. In 1993,[11] none of the responding institutions discontinued AMP within 24 h and in 2003,[7] this had increased to only 3.1%. Conversely, 10.4% of the responding institutions in the present survey discontinued AMP within 24 h after surgery. Most of the responding institutions continued to administer AMP for 47–72 h. This is because the Japa-

Table 3. Oral administration of nonabsorbable antimicrobial agents in colorectal surgery

Type	*n* (%)
Metronidazole+KM	25 (29.8)
Metronidazole+PL-B	1 (1.2)
Metronidazole+fluoroquinolones	1 (1.2)
KM+EM	7 (8.3)
Metronidazole	4 (4.8)
KM+PL-B	1 (1.2)
KM+fluoroquinolones	1 (1.2)
PL-B+cephalosporins or penicillins	1 (1.2)
KM	25 (29.8)
PL-B	2 (2.4)
Fluoroquinolones	10 (11.9)
Cephalosporins or penicillins	1 (1.2)
No answer	5 (6.0)

KM, kanamycin; PL-B, polymyxin B; EM, erythromycin

Table 4. Adherence to recommendations for antimicrobial prophylaxis in Japan

Perioperative procedure	Recommendation	Adherence
Antimicrobial prophylaxis		
Timing	Started within 1 h before surgery	668/714 (93.6%)
Duration	Stopped within 24 h after the operation	74/712 (10.4%)
Dose	Every 8 h	43/638 (6.7%)
Agent	Second-generation cephalosporins	707/845 (83.7%)
	Second-generation cephalosporins with antianaerobic activity	547/845 (64.7%)
Mechanical bowel preparation	(Controversial)	
	No preparation	8/713 (1.1%)
Preoperative oral antibiotics	(Controversial)	
	Used	84/714 (11.7%)
Duration	One day before the operation	66/84 (78.6%)
Spectrum	Anaerobic+aerobic	34/84 (40.5%)

nese guidelines, which were jointly developed by the Japanese Association for Infectious Disease (JAID) and the Japanese Society of Chemotherapy (JSC), recommends continuing prophylaxis for up to 72 h after the operation. The JSSI is now conducting a randomized controlled trial to compare 24 h of prophylaxis with 72 h of prophylaxis. The duration of AMP may be changed by the results of this trial.

Many antimicrobial regimens are effective in preventing SSI. In general, the AMP agents include older, relatively narrow-spectrum agents such as the first- and second-generation cephalosporins. In colorectal surgery, the antimicrobial agents need a broad spectrum of activity to target Gram-positive, Gram-negative, and anaerobic bacteria.

Because intravenous metronidazole was not available in Japan, the combination of cefazolin and metronidazole was not used in any hospital in this study. Cefmetazole and flomoxef, second-generation cephalosporins, show a broad spectrum of activity and are used widely in elective colorectal surgery in Japan. These agents have a similar antimicrobial spectrum to cefotetan and are recommended based on the JAID/JSC guidelines. We found that about 65% of the respondents used prophylactic antimicrobial agents consistently with the current guidelines.

The CDC guidelines recommend oral nonabsorbable antimicrobial agents, in divided doses the day before surgery, in addition to intravenous antibiotics during colorectal surgery.[1] In North America, antibiotics are often administered by a combination of oral and intravenous routes.[14] In 2003, Zmora et al. conducted a survey of 515 members of the American Society of Colon and Rectal Surgeons and found that 49% felt prophylactic oral antibiotic to be essential, 41% deemed it doubtful, and 10% considered oral prophylaxis unnecessary. Despite these statements, 75% of the surgeons routinely prescribed oral antibiotics, 11% prescribed them selectively, and only 13% omitted oral prophylaxis.[15] By contrast, most surgeons in Europe and Asia now use intravenous antibiotics alone.[16,17] In 1993, 75.4% of responding institutions in Japan gave preoperative nonabsorbable oral antibiotics, whereas in 2003 80.7% gave mechanical bowel preparation only, without preoperative oral antibiotics.[9] In the present survey, only 12% of the responding institutions administered oral antibiotics. In a previous randomized clinical trial, preoperative oral antibiotics were not deemed necessary for the prevention of SSI in elective colorectal surgery.[18,19] The use of preoperative prophylactic oral antibiotic is controversial, although the CDC guidelines recommend oral antimicrobial agents. In selecting the oral antibiotics for patients undergoing colorectal surgery, 40.5% of the hospitals stated that they selected drugs effective against aerobic and anaerobic organisms. We found that Japanese Surgeons selected drugs that were not effective enough against anaerobic organisms.

In Japan, the appropriate use of AMP has improved over the last decade. Nguyen et al. found that the appropriate use of AMP decreased the incidence of SSI.[20] The Japanese Society of Environmental Infections established the Japanese Nosocomial Infection Surveillance (JNIS) system and initiated SSI surveillance in Japan in 1999.[21] According to a JNIS report, the incidence of SSI after colon surgery and rectal surgery decreased from 16.7% to 12.7% and from 19.4% to 16.3%, in 2001 versus 2008. However, an association between the appropriate use of AMP and clinical outcomes such as SSI has not been confirmed. We did not survey the incidence of SSI in this study. Further studies, including a retrospective cohort study, are needed to clarify the relationship between the appropriate use of AMP and a decreased incidence of SSI in Japan.

In conclusion, the appropriate use of AMP in colorectal surgery was found to be lacking in the certified institutions in Japan. It is concerning that many of the institutions administer AMP for longer than recommended. Although a worldwide consensus on preoperative colon preparation has not been reached, the usefulness of oral AMP is not underlined in Japan. The JSSI is now conducting a randomized controlled trial to investigate the optimal duration of AMP to gather evidence specific to Japan. We expect that the duration of AMP in Japan will be changed dramatically by the results of this trial.

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