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Pain management using acetaminophen throughout postoperative course of laparoscopic colorectal surgery: A case-matched control study

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HIGHLIGHTS

- Multimodal analgesia with acetaminophen was effective after laparoscopic surgery.
- Adverse events were less frequent with acetaminophen than epidural anesthesia.
- Frequency and variability of rescue use were lower with acetaminophen than epidural.

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ABSTRACT

Backgroud: The main advantage of laparoscopic surgery is that it is minimally invasive because of the use of small incisions. An approach using small incisions offers many benefits including attenuation of surgical wound pain. However, the presence of postoperative pain may undermine the advantages of laparoscopic surgery as a minimally invasive technique. In addition, perioperative pain management is an important factor affecting recovery after surgery. This study investigated the usefulness of a multimodal approach to postoperative pain management with acetaminophen as a baseline analgesic after minimally invasive laparoscopic colorectal surgery.

Materials and methods: The study included 40 patients who underwent laparoscopic colorectal surgery for colorectal cancer. 20 patients received acetaminophen as a baseline analgesic for postoperative pain management and 20 received epidural anesthesia.

Results: The urethral catheter could be removed earlier in the acetaminophen group (2.1 ± 0.22 days postoperatively) compared with the epidural group (4.1 ± 0.45days postoperatively). The frequencies of vertigo were significantly lower in the acetaminophen than epidural group (10.0% and 45.0%, respectively). The frequencies of the use of analgesics on an as-needed basis for postoperative pain relief as well as the variabilities in these frequencies, although not significantly different between the acetaminophen and epidural groups, were lower in the acetaminophen group than the epidural group.

Conclusion: We herein demonstrated that postoperative pain management with acetaminophen as a baseline analgesic, and without the use of epidural anesthesia, is a safe and useful analgesic modality.

1. Introduction

The application of laparoscopic surgery has rapidly become widespread since the first laparoscopic cholecystectomy was reported in 1990 [1] and successful performance of laparoscopic colorectal surgery was described in 1991 [2]. The main advantage of laparoscopic surgery is that it is minimally invasive because of the use of small incisions. An approach using small incisions offers many benefits including not only improvement of cosmetic outcomes and attenuation of surgical wound pain but also early ambulation, early initiation of oral intake due to early return of normal bowel function, and early rehabilitation [3–7].

However, the presence of postoperative pain may undermine

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the advantages of laparoscopic surgery as a minimally invasive technique. In addition, perioperative pain management is an important factor affecting recovery after surgery [8–11]. Consequently, the concept of multimodal analgesia has become widespread; this involves the use of different classes of analgesics with different mechanisms of action to achieve an increased total analgesic effect with the use of smaller doses and a concomitant reduction in side effects [12]. Modalities used for perioperative pain management include opioids, epidural anesthesia, peripheral nerve block, non-steroidal anti-inflammatory drugs (NSAIDs), and acetaminophen. These modalities differ in analgesic effects according to the type of pain (e.g., pain at rest, movement-related pain, and visceral pain) and the degree of invasiveness of the surgical techniques as well as in side effects.

This study investigated the usefulness of a multimodal approach to postoperative pain management with acetaminophen as a baseline analgesic, and without the use of epidural anesthesia, after minimally invasive laparoscopic colorectal surgery.

2. Materials and methods

2.1. Patients

The study included 83 patients who underwent laparoscopic colorectal surgery for colorectal cancer at the Department of Surgery, School of Medicine, Kitasato University, Japan, from August 2015 through December 2015. This study selected 40 patients were matched for age, sex, procedure, body-mass index, the operation time, and the amount of blood loss. Of the 40 patients, 20 received acetaminophen as a baseline analgesic for postoperative pain management and 20 received epidural anesthesia (Table 1). Endoscopy, computed tomography, and barium enema were performed for the purpose of preoperative diagnosis in all patients.

2.2. Anesthesia and perioperative pain management

Fig. 1 All the patients received general anesthesia during the surgical procedure. Propofol, remifentanil, fentanyl, and muscle relaxants were used for induction of anesthesia, and sevoflurane, remifentanil, fentanyl, and muscle relaxants were used for maintenance of anesthesia.

The patients who received acetaminophen as a baseline analgesic for postoperative pain management (Ace group) were administered acetaminophen 1000 mg intravenously every 6 h from at least 30 min before completion of the surgery until postoperative day 2; for patients weighing less than 50 kg, the acetaminophen dosage did not exceed a maximum single dose of 15 mg/kg or a maximum daily dose of 60 mg/kg. In addition, 15 mL ropivacaine 5% was injected locally into the anterior surface of the anterior sheath of the rectus abdominis muscle at the umbilical wound site during abdominal closure. Continuous intravenous patient-controlled analgesia (IVPCA; continuous intravenous infusion of 12 mL fentanyl [600 μg] and 36 mL saline at a rate of 2 mL per hour) and intravenous NSAIDs were used on an as-needed basis for pain control until postoperative day 2. Oral NSAIDs were administered long term from postoperative day 2.

The patients who received epidural anesthesia as a baseline analgesic modality for postoperative pain management (Epi group) were also managed with this anesthetic modality during the surgical procedure. For postoperative pain management in the Epi group, continuous patient-controlled epidural analgesia (PCEA; continuous epidural infusion of 280 mL anapeine 0.2% and 8–10 mL

Table 1
Patients backgrounds.

	Ace group (n = 20)	Epi group (n = 20)	*p-value*
Age (years, mean ± SD)	64.9 ± 9.0	66.1 ± 11.4	*0.405*
Sex (Male/Female)	11/9	11/9	*1.00*
Procedure (Colon/Rectum)	8/12	8/12	*1.00*
BMI	22.7 ± 3.1	21.5 ± 2.7	*0.112*
Operation time (min., mean ± SD)	254.2 ± 121.8	240.4 ± 77.7	*0.815*
Blood loss (g, mean ± SD)	22.1 ± 42.7	19.8 ± 38.2	*0.897*

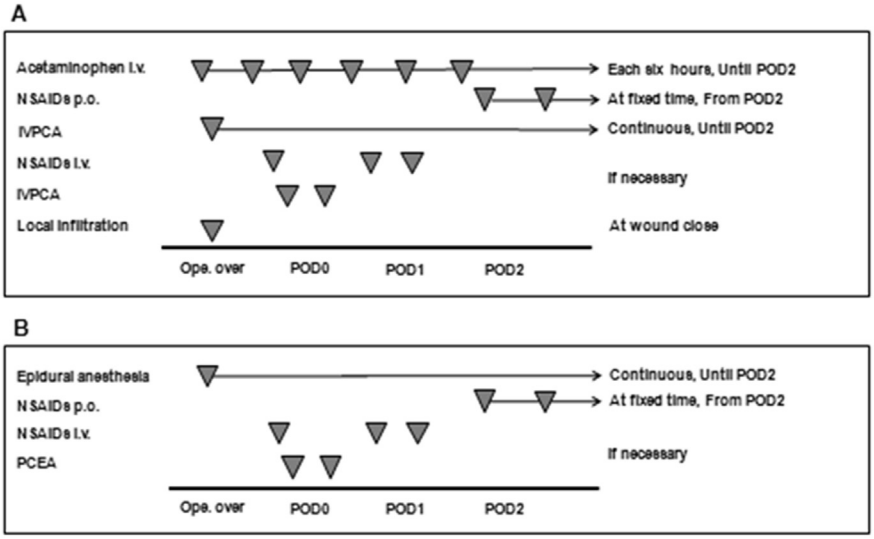

Fig. 1. Protocols of postoperative pain control (A) Acetaminophen using group, (B) Epidural anesthesia group.

fentanyl at a rate of 4–5 mL per hour) and intravenous NSAIDs were used on an as-needed basis for pain control until postoperative day 2. Oral NSAIDs were administered daily from postoperative day 2.

Pentazocine may antagonize the effects of drug combination and therefore was contraindicated in the Ace and Epi groups.

2.3. Surgical technique

Laparoscopic surgery was performed using a transumbilical open approach with the patient in the lithotomy position. A 12 mm trocar was inserted in the umbilicus and pneumoperitoneum was created. In patients with right-sided colon cancer, 5 mm trocars were inserted in the left and right lateral abdominal regions, left lower abdominal region, and the midline of the lower abdomen. In patients with left-sided colon cancer and those with rectal cancer, 5 mm trocars were inserted in the left and right lateral abdominal regions and left lower abdominal region, and a 12 mm trocar was inserted in the right lower abdominal region. After dissection and mobilization of the mesentery through a medial approach and subsequent ligation and division of the vasa vasorum, lymphadenectomy was performed. Subsequently, the intestine was exteriorized through the umbilical wound and the tumor was removed. Gastrointestinal anastomosis was performed using a double-stapling or functional end-to-end technique.

2.4. Outcomes

The outcome measures included the factors influencing postoperative recovery (including the times to first passing gas, first postoperative ambulation, and urethral catheter removal), frequencies of adverse events associated with pain management (including nausea, hypotension, vertigo, and numbness of the legs), and frequencies of use of postoperative analgesics on an as-needed basis.

2.5. Statistical analysis

Results were expressed as mean, standard deviation, and percentage. Statistical analysis was performed using JMP Pro 11.0 (SAS Institute Inc., Cary, NC, USA).

3. Results

3.1. Influence for postoperative recovery

Comparison of the factors influencing postoperative recovery between the Ace and Epi groups showed no intergroup difference in the times to first passing gas and first postoperative ambulation. In contrast, the urethral catheter could be removed earlier in the Ace group (2.0 ± 0.2 days postoperatively) compared with the Epi group (4.1 ± 0.4 days postoperatively) (Table 2).

3.2. Adverse events

Comparison of the adverse events associated with pain management, which can delay early recovery after surgery, between the Ace and Epi groups showed that the frequencies of all adverse events evaluated in this study, including nausea, hypotension, vertigo, and numbness of the legs, were lower in the Ace group than the Epi group. The frequencies of vertigo were significantly lower in the Ace than Epi group (10.0% and 45.0%, respectively) (Fig. 2).

3.3. As-needed analgesics

The frequencies of the use of NSAIDs, PCEA, and IVPCA on an as-needed basis for postoperative pain relief as well as the variabilities in these frequencies, although not significantly different between the Ace and Epi groups, were lower in the Ace group than the Epi group (Fig. 3).

4. Discussion

This study investigated the usefulness of a multimodal approach to postoperative pain management with acetaminophen as a baseline analgesic, and without the use of epidural anesthesia, after minimally invasive laparoscopic colorectal surgery. Comparison of the factors influencing postoperative recovery between the Ace and Epi groups revealed that the time of urethral catheter removal, associated with delay in ambulation, was earlier in the Ace group than Epi group. In addition, the frequencies of adverse events possibly associated with epidural anesthesia and opioids, and the frequencies of use of analgesics on an as-needed basis for postoperative pain as well as variability in these frequencies, were lower in the Ace group than Epi group.

Laparoscopic surgery was introduced in 1990 with the performance of the first laparoscopic cholecystectomy, and is currently widely performed as a minimally invasive procedure producing excellent cosmetic outcomes in patients with various conditions

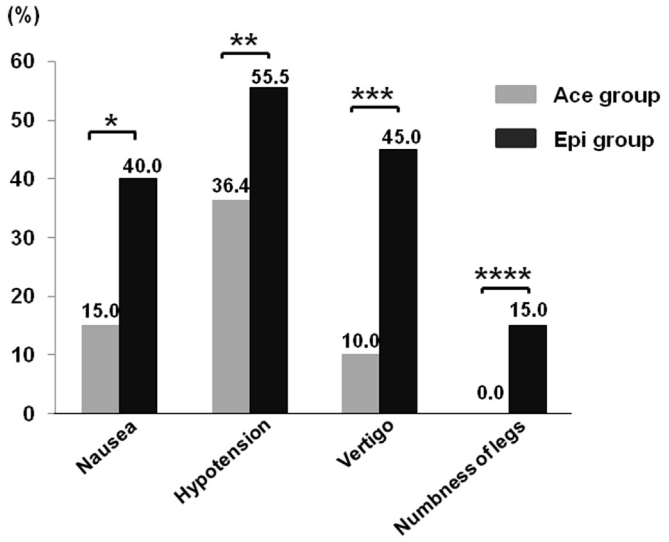

Fig. 2. Frequency of adverse events possibly associated with pain management, which can delay early postoperative recovery *$p < 0.078$, **$p < 0.334$, ***$p < 0.008$, ****$p < 0.152$.

Table 2
Influence for postoperative recovery.

	Ace group (n = 20)	Epi group (n = 20)	*p*
First passing gas (days, mean ± SD)	0.95 ± 0.76	0.80 ± 0.77	*0.546*
First postoperative rising (days, mean ± SD)	1.2 ± 0.52	1.1 ± 0.31	*0.601*
Remove of urethral catheter (days, mean ± SD)	2.1 ± 0.22	4.1 ± 0.45	*0.000*

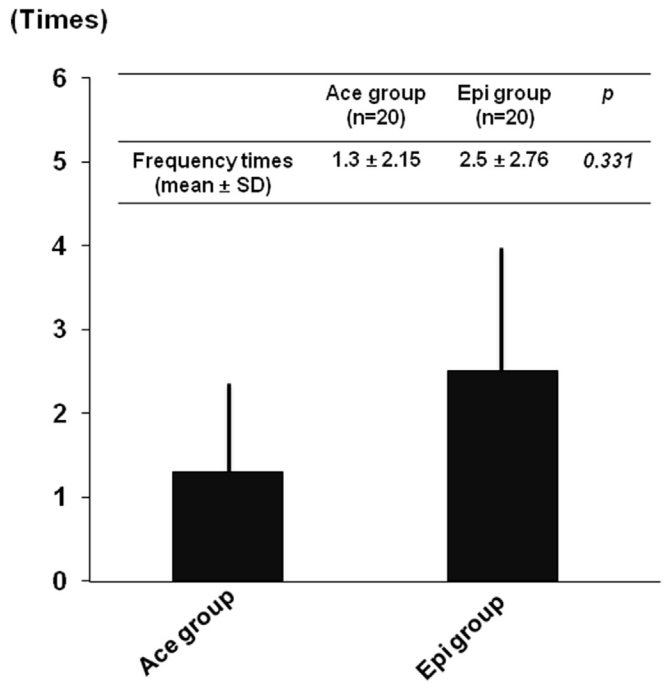

Fig. 3. Frequencies of use of NASIDs, PCEA, and IVPCA on an as-needed basis for postoperative pain relief.

[1]. Laparoscopic surgery yields not only excellent cosmetic outcomes associated with the use of small incisions but also many other benefits including less surgical wound pain than with open surgery, early ambulation, and early return of normal bowel function [3–7].

However, postoperative pain may undermine the advantages of laparoscopic surgery as a minimally invasive technique, and perioperative pain management is an important factor contributing to enhanced recovery after surgery [8–11]. Epidural analgesia is commonly used to manage postoperative pain after open surgery, and its usefulness has been demonstrated [13]. However, postoperative pain management with epidural analgesics is associated with marked changes in circulatory dynamics and frequent use of pressor drugs throughout the perioperative period. Previous study revealed nausea and vomiting in approximately 50%, and motor paralysis and numbness of the lower extremities in approximately 30%, of patients treated with this modality, as well as frequent observation of serious complications including dural puncture and epidural hematoma formation [14–17]. Such adverse events attributable to this pain management modality can apparently delay early recovery after surgery.

Successful control of pain after laparoscopic surgery has recently been reported with the use of continuous intravenous fentanyl infusion combined with oral analgesics [14] or particularly acetaminophen [18]. This finding was attributed to the presence of less surgical wound pain. In addition, circulatory dynamics remained stable. The authors of these studies therefore recommend that epidural analgesia not be used in patients undergoing laparoscopic surgery.

Multimodal analgesia is pain management with non-opioid analgesics as baseline analgesics in addition to local anesthesia or regional anesthesia. Advantages of this technique are increased total effects of different classes of analgesics through their different mechanisms of action, together with the use of smaller doses with a concomitant reduction in side effects [12]. Non-opioid analgesics used for multimodal analgesia include NSAIDs and acetaminophen. These modalities differ in analgesic effects according to the type of pain, such as pain at rest, movement-related pain, and visceral pain, as well as in side effects.

Acetaminophen exerts antipyretic effects through its direct action on the hypothalamus as well as analgesic effects through its direct action on the thalamus and cortex. Although acetaminophen is not fast-acting and is relatively ineffective when used alone, its effects on renal function and gastrointestinal mucosal injury are negligible. Acetaminophen is therefore recommended as a modality for postoperative pain management in patients undergoing laparoscopic surgery, elderly patients, and patients with renal disorders [13,19,20]. This study verified the usefulness of postoperative pain management with acetaminophen as a baseline analgesic, and without the use of epidural anesthesia, after laparoscopic colorectal surgery.

Our study revealed that the variability in the frequencies of use of analgesics on an as-needed basis differed between the two groups. This finding was considered to result from differences in epidural anesthesia technique between operators as well as physique between patients. These factors do not affect pain management with acetaminophen as a baseline analgesic. This observation indicates that acetaminophen analgesia can offer stable analgesic efficacy.

We herein demonstrated that postoperative pain management with acetaminophen as a baseline analgesic, and without the use of epidural anesthesia, is a safe and useful analgesic modality. We predict that, in future, widespread application of this modality for pain management may not only enhance the advantages associated with the minimally invasive approach in laparoscopy and reduce complications after gastrointestinal anastomosis but also benefit the patient in terms of patient safety.

Ethical approval

None required.

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None received.

Author contribution

Masanori Naito: designed the study, performed procedures, collected data, composed the manuscript.

Masahiko Watanabe: reviewed the manuscript.

Hirohisa Miura, Takatoshi Nakamura, Takeo Sato, Takahiro Yamanashi and Atsuko Tsutsui: performed procedures.

Conflicts of interest

None to declare.

Guarantor

Masanori Naito, First Author.
Masahiko Watanabe, Senior Author.

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