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ORIGINAL ARTICLE

Comparative Efficacy of Mechanical Patient-Controlled Analgesia Pump Operated in Patient Optimizing Background Infusion Mode and Conventional Nonmechanical Pump after Laparoscopic Surgery

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Objective: The aim of this study was to evaluate the efficacy and side effects of the mechanical patient-controlled analgesia (PCA), pumps operated in patient optimizing background infusion (POBI) mode, compared with the conventional nonmechanical PCA after laparoscopic gynecologic surgery.

Methods: In total, 211 patients were randomized to nonmechanical pump (n = 106, group A) or mechanical pump (n = 105, group P) postoperative pain treatment groups. A single blinded observer evaluated and recorded postoperative nausea and vomiting (PONV) score as well as the background infusion rate, Numeric Rating Scale (NRS), use of an additional antiemetic or analgesic, degree of sedation, and other side effects at 30 minutes, 2 hours, 8 hours, and 24 hours postoperatively. The degree of patient satisfaction was evaluated at 2 and 24 hours postoperatively.

Results: There was no significant difference in the overall NRS score between the two groups. However, the use of rescue analgesics was significantly higher in group A (P = 0.007). The incidence of PONV did not significantly differ between the two groups at 0.5 hours postoperatively; however, at 2 hours, it was significantly higher in group P than in group A (P = 0.003). In contrast, the incidence of PONV was significantly lower in group P than in group A at 24 hours postoperatively (P = 0.033). No significant group difference was observed in patient satisfaction.

Conclusion: With an appropriate waiting time, a mechanical pump operating in POBI mode could be an effective PCA pump to reduce postoperative pain and side effects.

Keywords: Patient-controlled analgesia; Fentanyl; Gynecologic surgical procedures; Infusion pumps; Pain management; Postoperative pain; Postoperative nausea and vomiting

INTRODUCTION

Appropriate pain control not only decreases the frequency of postoperative complications but also helps rapid recovery [1]. The degree of patient satisfaction with intravenous patient-controlled analgesia (IV-PCA) is high compared to the conventional method involving the administration of an analgesic by a medical practitioner according to need [2-4].

Postoperative pain degree is highly variable according to the site, type, and method of operation. In addition, the minimum effective plasma concentration of fentanyl, used in the present study, is differed among individuals (up to 5 times) the dose should be carefully determined [5]. Therefore, it is important to provide a sufficiently high level of pain control autonomy to patients. However, nonmechanical PCA pumps in which the drug dose or injection method is set up in advance do not allow a sensitive response to the pain of individual patients.

Fentanyl has desirable properties as an IV-PCA drug because its analgesic effect is expressed rapidly, starting within 30 seconds after administration and reaching a peak at 5 minutes; it is rapidly and extensively redistributed in the body, has a short duration, and does not produce any active metabolites that cause respiratory depression [6,7]. Although fentanyl is ideal for IV-PCA, it displays all opioid-related adverse effects, including nausea, vomiting, and

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pruritus at clinically relevant doses [8].

Mechanical PCA pump (PAINSTOP; Unimedics Co. Ltd., Seoul, Korea) is a newly released mechanical PCA pump that allows for pain control by patients via a unique mode that the nonmechanical PCA pumps do not have, which is the patient optimizing background infusion (POBI) mode. In this mode, when a patient presses the demand bolus button because of severe pain, an additional bolus dose is injected, and the background infusion rate is automatically increased as much as the set value to administer more analgesic. In the opposite case, the background infusion rate can also be automatically decreased to administer less analgesic. In this way, the patient can sensitively respond to the patient's pain state. In addition, as the mode allows setting the maximum and minimum background infusion rate according to the postoperative time, fatal complications that may occur due to excessive use of opioids are prevented. Therefore, we anticipated that giving a sufficiently high level of pain control autonomy to patients using the POBI mode on a mechanical pump may decrease postoperative nausea and vomiting (PONV), and increase the analgesic effect and patient satisfaction compared to the conventional nonmechanical PCA.

The purpose of the present study was to compare the analgesic effect, the quantity of PCA used, PONV, and patient satisfaction after a laparoscopic gynecologic surgery between a nonmechanical pump and the mechanical pump operated in POBI mode.

MATERIALS AND METHODS

1. Ethical approval

The present study was conducted after acquiring approval from the Hospital Ethics Committee of Soonchunhyang University Chenona Hospital (approval no., 2018-02-006) and registered on an international clinical trials registry platform (KCT0003633). Written informed consent was obtained from eligible patients.

2. Study population

The trial included 232 female patients between 18 and 65 years of age with the American Society of Anesthesiologist physical status of Ⅰ or Ⅱ who were scheduled to undergo laparoscopic gynecologic surgery and wanted to receive postoperative IV-PCA. Patients with chronic obstructive pulmonary disease or brain damage; those who had abused drugs or who had hypersensitivity to the drugs used for PCA, such as fentanyl and ketorolac; those who had kidney or liver disease that may cause a pharmacokinetic or pharmacodynamic abnormality with respect to the drug action; and those who failed to understand the PCA method or who were unable to communicate were excluded from the present study.

3. Study design

On the day before the surgery, written informed consent was provided by the patients after explaining the purpose of the study, how to use the PCA, how to complete the Numeric Rating Scale (NRS), and side effects. The patients were randomly allocated to different IV-PCA groups: group A, the nonmechanical PCA pump group (ANAPA; E-WHA Meditech Inc., Goyang, Korea); and group P, the mechanical PCA pump group (PAINSTOP; Unimedics Co. Ltd.).

All patients arrived in the operating room, without being administered a pre-anesthetic after venous access was secured with an 18G catheter. An electrocardiograph, noninvasive blood pressure monitor, and pulse oximeter were attached to the patient in the operating room. Propofol (2 mg/kg) and rocuronium bromide (0.8 mg/kg; Rocnium; Hanlim Pharm. Co. Ltd., Seoul, Korea) were administered intravenously to induce and maintain anesthesia. After endotracheal intubation, mechanical ventilation was performed by supplying oxygen and air at a FiO_2 of 0.4 and sevoflurane (end-expiratory concentration of 2–2.5 vol%) to maintain end-expiratory carbon dioxide of 35–40 mm Hg. The sevoflurane concentration was controlled so that the variation in blood pressure and heart rate remained within 20% of the pre-anesthetic measurements to maintain an appropriate anesthetic depth. Dexamethasone (5 mg) was injected intravenously immediately after induction of anesthesia to prevent PONV. All surgeries were performed by the same surgeon. The anesthetics were discontinued after the surgery, and pyridostigmine and glycopyrrolate were administered to reverse muscle relaxation. Extubation was performed after checking for sufficient recovery of patient consciousness and spontaneous breathing.

Following extubation, fentanyl (700 μg), ketorolac (150 mg), and ramosetron (0.6 mg) were mixed with saline to prepare a 100 mL solution, which was administered to the group A patients using the nonmechanical pump at a background infusion rate of 2 mL/hr, in a demand bolus dose of 0.5 mL and with a lockout interval of 15 minutes set in advance. Loading doses of fentanyl (100 μg) and ketorolac (30 mg) were administered for postoperative pain control, and ramosetron (0.3 mg) was administered to prevent PONV.

The same doses of the drugs as used in group A were mixed and administered by the mechanical pump at an initial background infusion rate of 6 mL/hr in a demand bolus dose of 2 mL at a lockout interval of 7 minutes for group P. The waiting time was 60 minutes. The pump was set up to inject an additional bolus dose and increase the background infusion rate by 1 mL/hr each time the patient pressed the bolus button due to severe pain, or to decrease the background infusion rate by 0.5 mL/hr if the patient did not press the bolus button during the 60 minutes wait time. In addition, the maximum and minimum background infusion rates were set as 10 and 4 mL/hr, respectively during the first 2 postoperative hours, decreasing to 6 and 1 mL/hr during postoperative 2–8 hours, and decreasing to 4 and 1 mL/hr thereafter. The loading dose for postoperative pain control was the same as that for group A.

A single blinded observer evaluated and recorded the PONV score as well as the background infusion rate, NRS, use of an additional antiemetic or analgesic, degree of sedation, and other side effects at 30 minutes, 2 hours, 8 hours, and 24 hours postoperatively. The degree of patient satisfaction was evaluated at 2 and 24 hours postoperatively.

Pain was rated using the NRS, where 0 = no pain and 10 = unbearably severe pain. The patients were asked to press the bolus button if they wanted additional pain relief when the NRS score was in the range of 3 to 5, representing moderate pain, even though a predetermined dose of the analgesic was being administered. Fentanyl was administered intravenously at a dose of 1 μg/kg if the patient wanted additional pain control when the NRS score was 5 or higher, representing high-intensity pain.

PONV was evaluated on a 4-point scale where 0 = no PONV, 1 = nausea, 2 = severe nausea, and 3 = vomiting. When the PONV score was 2 or higher, 10 mg metoclopramide was administered

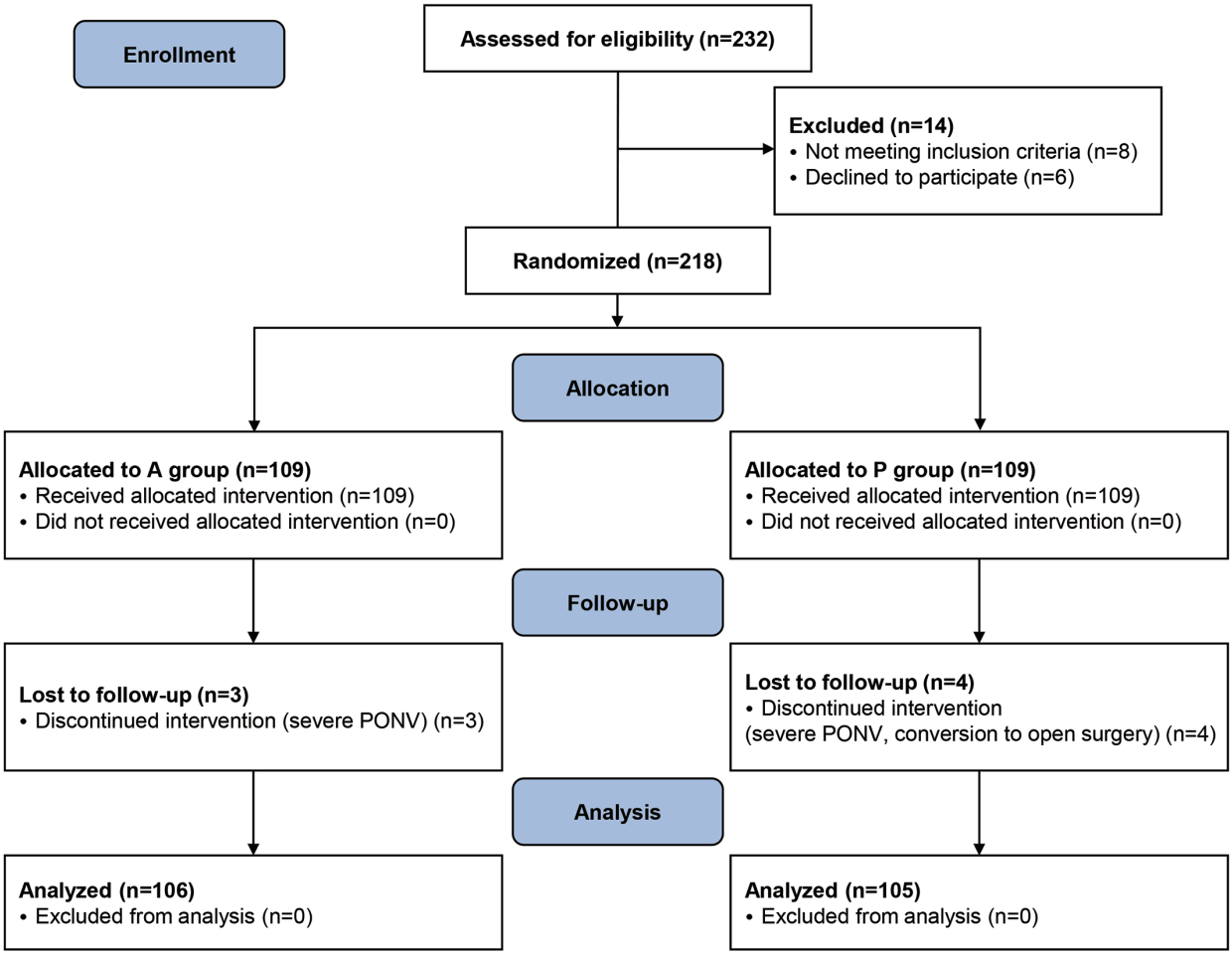

Fig. 1. CONSORT (Consolidated Standards of Reporting Trials) flow diagram. PONV, postoperative nausea and vomiting.

intravenously.

Pheniramine (25 mg) was administered intravenously to patients who had an itch and wanted treatment. The observed side effects included dizziness, pruritus, itch, constipation, and respiratory depression.

Sedation was evaluated by the Modified Observer's Assessment of Alertness/Sedation (MOAA/S) scale, where 5 = patient immediately responded to their name being spoken and was orientated, 4 = patient provided a lethargic response to their name being spoken, 3 = patient responded lethargically to their name being spoken repeatedly, 2 = patient responded only after mild prodding or shaking, 1 = patient responded only after a painful squeeze, and 0 = patient did not respond. Respiratory depression was defined as 8 or fewer breaths per minute. PCA was immediately blocked in cases with a MOAA/S scale score of 1 or lower, or if 0.01 mg/kg naloxone was administered intravenously for respiratory depression.

The degree of patient satisfaction was determined at 2 and 24 hours postoperatively as "very satisfied" "satisfied," "moderate," or "disappointed."

Previous studies were reviewed to estimate the required number of study subjects [9]. The incidence of PONV at 24 postoperative hours was 0.143, and our study was a pilot study, so it was set to be 0.05 to indicate a clinically significant difference (d = 0.1). With a significance level (α) of 0.05 (one-sided), power (1–β) of 0.8, and an expected dropout rate of 10%, the number of subjects needed for each group was finally calculated as 116.

The statistical analysis was performed using PASW SPSS software for Windows ver. 18.0 (SPSS Inc., Chicago, IL, USA). The data are expressed as mean ± standard deviation. The demographic data were analyzed by Pearson's chi-square test or Student t-test. The generalized estimating equation approach was used to compare the quantity of IV-PCA used over 24 hours, the background infusion rate, and the NRS score at rest between the two groups. Pearson's chi-square test or Fisher's exact test was performed to compare the frequency of side effects and the degree of satisfaction between the two groups.

RESULTS

In total, 232 patients were screened, among whom 218 were enrolled in the study and divided randomly into two groups. Of the study patients, three in group A and four in group P were excluded from the study. Data obtained from the remaining 211 patients

Table 1. Demographic data and anesthesia characteristics of the patients

Characteristic	Group A[a]	Group P[b]	P-value
No. of patients	106	105	
Age (yr)	45.3 ± 6.3	45.5 ± 5.9	0.775
ASA physical status			0.307
I	81	86	
II	25	19	
Type of operation			0.472
Laparoscopic supracervical hysterectomy	84 (79.2)	81 (77.1)	
Laparoscopic myomectomy	18 (17.0)	16 (15.2)	
Total laparoscopic hysterectomy	4 (3.8)	8 (7.6)	
Smoking status			0.238
Smoker	12	7	
Nonsmoker	94	98	
History of motion sickness or PONV	29 (27.4)	38 (36.2)	0.168
Height (cm)	157.4 ± 5.2	158.1 ± 4.6	0.315
Weight (kg)	60.0 ± 8.5	61.5 ± 8.7	0.210
Body mass index (kg/m^2)	24.2 ± 3.1	24.6 ± 3.2	0.421
Total fluid (mL)	329.3 ± 204.1	313.1 ± 197.0	0.560
Duration of surgery (min)	58.4 ± 15.6	61.7 ± 15.7	0.130
Duration of anesthesia (min)	82.2 ± 15.6	84.5 ± 15.8	0.288

Values are presented as number, mean ± standard deviation, or number of patients (%). There were no significant differences between the two groups.
ASA, American Society of Anesthesiologists; PONV, postoperative nausea and vomiting; PCA, patient-controlled analgesia.
[a]ANAPA group: nonmechanical PCA pump group. [b]PAINSTOP group: mechanical PCA pump group.

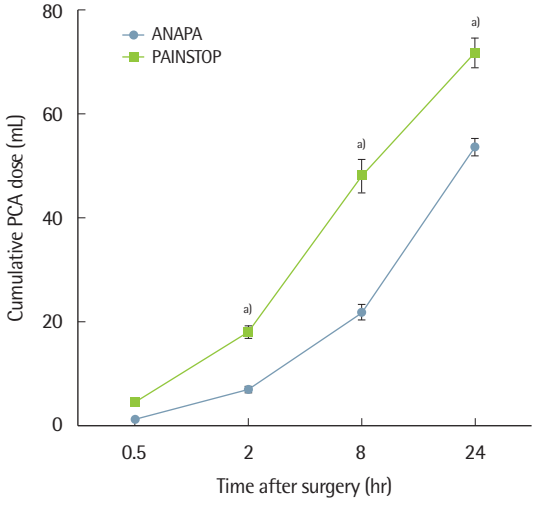

Fig. 2. Accumulated patient-controlled analgesia (PCA) consumption (mL) at 0.5–24 hours postoperatively (mean ± standard deviation). P-value was calculated by the generalized estimating equation approach. ANAPA group: nonmechanical PCA pump group; PAINSTOP group: mechanical PCA pump group.
[a]P < 0.001 for the interaction effect between group and time.

were analyzed, with 106 patients in group A and 105 patients in group P (Fig. 1).

Subjects were not significantly different in age, height, weight, operation duration, anesthesia duration, American Society of Anesthesiologist physical status, motion sickness, or smoking status (Table 1).

Accumulated PCA consumption was significantly higher in group P than in group A at 2, 8, and 24 hours postoperatively but not at 0.5 hours postoperatively (Fig. 2). The background infusion rate was significantly higher in group P than in group A at 0.5, 2, and 8 hours postoperatively. However, the background infusion rate of group P was significantly lower at 24 hours postoperatively than that of group A (Fig. 3).

The NRS at rest did not significantly different between the two groups at any time point, including 30 minutes, 2 hours, 8 hours, and 24 hours postoperatively (Fig. 4). However, additional use of rescue analgesics was significantly higher in group A (7.5%) than that of group P (0%) at postoperative 0.5 hours (P = 0.007) (Table 2).

The PONV incidence was not significantly different between the two groups at 0.5 hours postoperatively; however, it was significantly higher in group P than in group A at 2 hours postoperatively (P = 0.003). In contrast, PONV incidence was significantly lower in group P than in group A at 24 hours postoperatively (P = 0.033) (Table 3). The rate of additional use of an antiemetic was not significantly different between the two groups (Table 2).

Dizziness occurred significantly higher in group A (Table 4). No significant difference was observed in sedation scores between the two groups. The degree of patient satisfaction at 2 and 24 hours postoperatively was not significantly different between the two groups (Table 5).

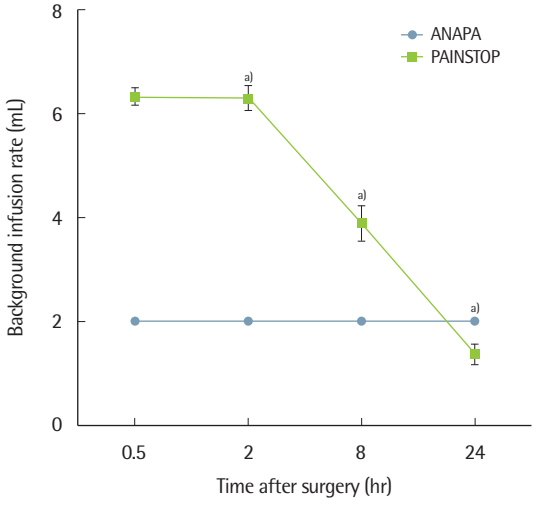

Fig. 3. Patient-controlled analgesia (PCA) background infusion rate (mL) at 0.5–24 hours postoperatively (mean ± standard deviation). P-value was calculated by the generalized estimating equation approach. ANAPA group: nonmechanical PCA pump group; PAINSTOP group: mechanical PCA pump group. [a]P < 0.001 for the interaction effect between group and time.

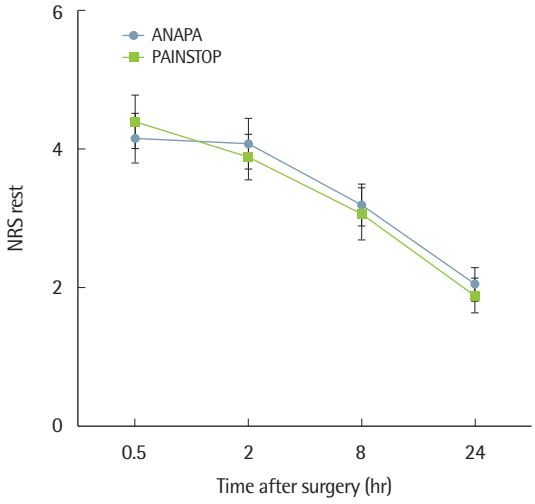

Fig. 4. Numeric rating scale (NRS, 0–10 mm) at rest 0.5–24 hours postoperatively (mean ± standard deviation). P-value was calculated by the generalized estimating equation approach. ANAPA group: nonmechanical PCA pump group; PAINSTOP group: mechanical PCA pump group.

Table 2. Use of rescue analgesics and antiemetics

Time after surgery (hr)	Group A[a] (n = 106)		Group P[b] (n = 105)		P-value	
	Analgesics	Antiemetics	Analgesics	Antiemetics	Analgesics	Antiemetics
0.5	8 (7.5)	0	0	0	0.007	-
2	2 (1.9)	0	0	1 (1.0)	0.499	0.475
24	0	2 (1.9)	0	0	-	0.499

Values are presented as number of patients (%).
PCA, patient-controlled analgesia.
[a]ANAPA group: nonmechanical PCA pump group. [b]PAINSTOP group: mechanical PCA pump group.

Table 3. Postoperative nausea and vomiting score

Time after surgery (hr)	Group A[a] (n=106)	Group P[b] (n=105)	P-value
0.5			0.052
0. None	98 (92.5)	88 (83.8)	
1. Queasy	8 (7.5)	17 (16.2)	
2. Severe nausea	0	0	
3. Vomiting	0	0	
2			0.003
0. None	96 (90.6)	70 (74.5)	
1. Queasy	10 (9.4)	23 (24.5)	
2. Severe nausea	0	1 (1.1)	
3. Vomiting	0	0	
24			0.033
0. None	91 (85.8)	97 (96.0)	
1. Queasy	13 (12.3)	4 (4.0)	
2. Severe nausea	2 (1.9)	0	
3. Vomiting	0	0	

Values are presented as numbers of patients (%).
PCA, patient-controlled analgesia.
[a]ANAPA group: nonmechanical PCA pump group. [b]PAINSTOP group: mechanical PCA pump group.

Table 4. Incidence (%) of adverse events

Adverse events	Group A[a] (n=106)	Group P[b] (n=105)	P-value
Dizziness	33 (31.1)	18 (17.5)	0.022
Drowsiness	5 (4.7)	10 (9.7)	0.188
Pruritus	3 (4.8)	9 (8.7)	0.080
Constipation	1 (0)	5 (4.8)	0.115

Values are presented as number of patients (%).
PCA, patient-controlled analgesia.
[a]ANAPA group: nonmechanical PCA pump group. [b]PAINSTOP group: mechanical PCA pump group.

Table 5. Patient Satisfaction at 2 and 24 hours postoperatively

Time after surgery (hr)	Group A[a] (n=106)	Group P[b] (n=105)	P-value
2			0.248
Very satisfied	5 (4.7)	4 (4.2)	
Satisfied	53 (50.0)	51 (53.1)	
Neutral	41 (38.7)	40 (41.7)	
Dissatisfied	7 (6.6)	1 (1.0)	
24			0.740
Very satisfied	15 (14.2)	17 (16.7)	
Satisfied	55 (51.9)	57 (55.9)	
Neutral	34 (32.1)	27 (26.5)	
Dissatisfied	2 (1.9)	1 (1.0)	

Values are presented as number of patients (%).
PCA, patient-controlled analgesia.
[a]ANAPA group: nonmechanical PCA pump group. [b]PAINSTOP group: mechanical PCA pump group.

DISCUSSION

The purpose of the present study was to compare the analgesic effect, the quantity of PCA used, PONV, and patient satisfaction after laparoscopic gynecologic surgery between the nonmechanical PCA pump currently used in our institution, and the newly released mechanical pump operated in POBI mode to grant patients' sufficient pain control autonomy.

PCA requires an appropriate drug infusion device. PCA pumps are either mechanical or nonmechanical. Mechanical PCA pumps have less portability and convenience compared to nonmechanical pumps. However, mechanical pumps have a higher drug infusion accuracy (±5%) than nonmechanical pumps (±15%) [10], allowing control of the demand bolus dose or the lockout interval in a relatively wide range, and providing information about drug injection history and the delivery-to-attempt ratio.

The nonmechanical pumps used in our institution are highly portable because of their small size and lightness. In addition, it does not require recycling or a complicated setting because the dose and injection mode are predetermined. The basic predetermined settings include a background infusion rate of 2 mL/hr, bolus dose of 0.5 mL, and lockout interval of 15 minutes; thus, patient autonomy in pain control may not be total. Group A used rescue analgesics more significantly than group P at postoperative 0.5 hours because a fentanyl bolus dose of 3.5 μg failed to decrease pain in the patients of group A sufficiently.

The initial background infusion rate of the mechanical pump was determined after several simulation experiments. Administering more analgesic than the predetermined dosage was considered risky because naloxone was administered for postoperative respiratory depression in one of the subjects and this subject was excluded from the final analysis. The overall quantity of PCA used was greater in group P than in group A (Fig. 2), which was expected in view of the higher background infusion rate and bolus dose and the shorter lockout interval of group P than group A. However, the overall NRS score and degree of patient satisfaction were not significantly different between the two groups, contrary to our expectations (Fig. 3). This may be related to the fact that group A patients more used the additional rescue analgesics at 0.5 hours postoperatively (8 versus 0 subjects, P=0.007), and none of the patients in group P. We thought that the use of rescue analgesics affected the results since fentanyl's duration of action usually lasts 2 to 4 hours after IV [7]. Kawamata et al. [11] showed that primary

hyperalgesia caused by sensitization of primary afferent nociceptors due to incision in an experimental incision model decreased at 2 hours after the incision and that secondary hyperalgesia causing pain in the area around the incision site decreased at 6 hours after the incision. In the present study also, the NRS was decreased significantly at postoperative 2 hours. The average NRS score was 2 at postoperative 24 hours in both groups. This indicates that postoperative pain after a laparoscopic gynecologic surgery becomes sufficiently bearable at 24 hours postoperatively, and more attention should be paid to the occurrence of PONV rather than postoperative pain (Table 3, Fig. 3).

Recent advances in surgery and anesthesia have led to a significant reduction in severe postoperative complications. Accordingly, anesthesiologists have focused on other issues of importance to the patients. Eberhart et al. [12] reported that among the common postoperative symptoms, avoidance of PONV (49%) is the key concern rather than control of postoperative pain (27%) after surgery. Still, PONV has been described as the Achilles heel of anesthesiologists, increasing medical costs and morbidity, delaying recovery and discharge, and even leading to readmission in severe cases [13]. It is not surprising that patients are ready to pay between US $56 to $100 for a hypothetical ideal antiemetic [14,15].

The most important risk factors for PONV are female gender, nonsmoking status, history of PONV, and intraoperative or postoperative use of an opioid [16,17]. In the present study, where most of the patients had at least three of the major risk factors mentioned above, dexamethasone and ramosetron were administered, as preventive antiemetics. Despite the administration of preventive antiemetics, the PONV incidence at 2 hours postoperatively was 9.4% in group A and 25.6% in group P. A better result could have been obtained if the waiting time of the mechanical pump POBI mode had been shorter to allow a more rapid response to the pain degree of each patient. The PONV incidence at 24 hours postoperatively was 4% in group P, which was significantly different from that of group A (12.3%). This may have occurred because the background infusion rate was high in group A, although postoperative pain decreased sufficiently at 24 hours postoperatively.

The sedation score was not significantly different between the two groups, which may be because the subjects in the present study were relatively healthy at the age of 65 years or less, with the American Society of Anesthesiologists physical status I–II.

The present study had the following limitations. First, a crossover design was lacking because patients were only exposed to one of the two pumps. Second, the waiting time set for the mechanical pump was too long to allow a rapid response to changes in patient status. Third, since only female patient undergoing the laparoscopic surgery participated in this study, male patients or patients undergoing open major surgery are required.

In conclusion, with an appropriate waiting time, mechanical pump operating in POBI mode could be an effective PCA pump to reduce postoperative pain and side effects.

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

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