

Omission of fentanyl during sevoflurane anesthesia decreases the incidences of postoperative nausea and vomiting and accelerates postanesthesia recovery in major breast cancer surgery

Gotaro Shirakami^{1,2}, Yuriko Teratani¹, Hajime Segawa², Shogo Matsuura², Tsutomu Shichino², and Kazuhiko Fukuda²

¹Day Surgery Unit, Kyoto University Hospital, Kyoto, Japan

Abstract

Purpose. Our purpose was to investigate the effect of omission of fentanyl during sevoflurane anesthesia on the incidences of postoperative nausea and vomiting and on postanesthesia recovery in female patients undergoing major breast cancer surgery.

Methods. Female patients (American Society of Anesthesiologists [ASA] physical status [PS] class I-II; age, 28–84 years) undergoing major breast cancer surgery were randomized to one of two anesthesia maintenance groups: sevoflurane-fentanyl anesthesia (SF; n=25) or fentanyl-free sevoflurane anesthesia (S; n=26). All patients were administered with propofol 2mg·kg⁻¹ intravenously for anesthesia induction, a laryngeal mask airway was placed, and they received rectal diclofenac and local infiltration anesthesia. Anesthesia was maintained with sevoflurane in oxygen-air and they breathed spontaneously. The patients in group SF received fentanyl 0.1 mg intravenously and those in group S received normal saline during anesthesia.

Results. Group SF revealed higher incidences of postoperative nausea (68% vs 27%) and vomiting (32% vs 8%) in the first 24 postoperative hours than group S. The median (25th–75th percentile) length of time from postanesthesia care unit (PACU) admission to ambulation was significantly longer in group SF (n = 23) at 195 min (158–219 min), than in group S, at 141 min (101–175 min). Two patients in group SF could not walk during the PACU stay.

Conclusion. Omission of fentanyl during sevoflurane anesthesia, combined with diclofenac and local infiltration anesthesia, decreases the incidences of postoperative nausea and vomiting and accelerates postanesthesia recovery in patients undergoing major breast cancer surgery.

Key words Postoperative nausea and vomiting · Sevoflurane · Fentanyl · Recovery from anesthesia · Breast cancer surgery

Address correspondence to: G. Shirakami This work was presented in part at the 49th Congress of the Japanese Society of Anesthesiologists, in Fukuoka. Received: January 20, 2006 / Accepted: April 11, 2006

Introduction

Breast cancer surgery performed under general anesthesia using a volatile anesthetic is associated with high incidences (33%-85%) of postoperative nausea and vomiting (PONV) [1-14]. Recently, not only minor breast operations, such as lumpectomy, but major operations, such as mastectomy, have been performed as ambulatory surgery or "drive-through mastectomy" in order to decrease healthcare costs and improve the patients' emotional and psychological well-being [11,15–17]. Unpleasant postoperative symptoms, especially pain and PONV, are the limiting factors in practicing ambulatory surgery [11,16,18-20]. Intractable pain and/or PONV not only distress patients but also delay patient recovery and discharge, lead to hospitalization, and increase healthcare costs. These symptoms may decrease patient satisfaction and acceptability of ambulatory surgery.

Opioids—potent analgesics—are frequently used for intra- and postoperative pain relief. However, the routine use of opioid analgesics is questioned in ambulatory surgery because of their adverse effects, including nauseant and emetic actions that delay patient recovery and require hospitalization [16,18,20,21]. To decrease the consumption and side effects of opioids, multimodal approaches, using local and/or regional anesthesia and nonsteroidal antiinflammatory drugs (NSAIDs) have been recommended in ambulatory anesthesia [17,18,20,21].

The aim of this study was to investigate the effect of the omission of fentanyl (the opioid analgesic most commonly used during surgical operations) during sevoflurane anesthesia on the incidence of PONV and on postanesthesia recovery and other clinical profiles in female patients undergoing major breast cancer surgery. Local infiltration anesthesia and an NSAID, with or without fentanyl, were delivered for pain relief during anesthesia. Our intention was to improve anesthetic

²Department of Anesthesia, Kyoto University Hospital, 54 Shogoin-Kawahara-cho, Sakyo-ku, Kyoto 606-8507, Japan

and perioperative care in major breast cancer surgery and to develop fast-track breast cancer surgery in our day surgery unit (DSU).

Patients and methods

Adult female patients (American Society of Anesthesiologists [ASA] physical status [PS] class I-II; age, 28–84 years), who were scheduled to undergo a major breast cancer operation (unilateral modified radical mastectomy or wide local excision with axillary lymph node dissection) under general anesthesia at the DSU, Kyoto University Hospital, were studied prospectively between June 2000 and October 2002. The operation was performed on an outpatient basis and planned overnight observation (23-h admission). Exclusion criteria were probe lumpectomy, bilateral operation, duration of operation less than 60 min, intraoperative blood loss more than 200 ml, re-operation required due to postoperative hemorrhage, ischemic heart disease, psychiatric disease, hepatic disease, renal disease, pulmonary disease, body mass index more than 30 kg·m⁻², coagulation disorder, pregnancy, hormonal therapy, and preoperative refusal of the procedures for 23-h admission. Written informed consent was obtained from each patient and their relative(s) at an outpatient preoperative evaluation clinic, and the protocol was approved by the ethics committee of our institute.

Patients were randomly assigned to one of two groups, using a sealed envelope technique: SF (sevoflurane-fentanyl) or S (fentanyl-free sevoflurane). All patients were admitted to our DSU in the morning on the day of surgery, after a fast of more than 6 h. In all patients anesthesia induction was scheduled at 9:00 am. An intravenous (IV) line was placed while the patient was in the preoperative preparation area in the DSU. No patient received sedative, antiemetic, or analgesic drugs before entry to the operation room in the DSU.

In all patients, anesthesia was induced with propofol 2 mg·kg-1 IV, and a laryngeal mask airway (LMA) was placed. Lidocaine 1 mg·kg⁻¹ was administered IV just before the propofol IV injection to decrease injection pain. All patients received a suppository (diclofenac sodium, 50 mg × 2; total, 100 mg) and local infiltration anesthesia (0.5% lidocaine, $200 \,\mathrm{mg} \times 2$; total, $400 \,\mathrm{mg}$) into the surgical field for pain relief before the start and the end of the operation. Surgeons who were blinded to the group allocation performed the local infiltration anesthesia. Anesthesia was maintained with sevoflurane in oxygen-air (inspiratory oxygen concentration, 45%) and the patients breathed spontaneously. Patients in group SF (n = 25) received fentanyl IV $(25 \mu g \times 4; total,$ 0.1 mg; at anesthesia induction, before skin incision, before axillary dissection, and before skin closure), and patients in group S (n=26) received the same volume of saline IV during anesthesia. Attending anesthesiologists were blinded to the fentanyl/saline allocation. Electrocardiography, noninvasive arterial blood pressure, arterial oxygen saturation (S_{PO_2}), end-tidal concentrations of carbon dioxide (ET_{CO_2}) and sevoflurane (ET_{SEV}), and respiratory rate were continuously monitored. The dose of inhaled sevoflurane, and the use of other drugs, such as nicardipine for hypertension (systolic blood pressure >180 mmHg lasting \geq 5 min), were adjusted according to the clinical variables by an attending anesthesiologist. No urinary catheters or surgical drains were inserted.

After surgery, patients emerged from anesthesia and the LMA was removed in the operation room. They were transported first to the postanesthesia care unit (PACU) and then to the stepdown recovery area (SRA) in the DSU. In the PACU and SRA, trained nursing staff, who were blinded to the group allocation, interviewed the patients and documented adverse events, including nausea (complaint of nausea without vomiting) and vomiting (muscular movements expelling gastric contents), and recorded, routinely, vital signs every 15-30 min. They noted the drugs administered and the times when patients drank fluids, ate a light meal, walked, voided, and were discharged from the PACU/ SRA. Patients were allowed to take fluid and a light meal if they desired. The IV line was removed if they could tolerate oral intake. Patients reported their pain intensity using a 100-mm visual analogue scale (VAS; 0mm, no pain; 100mm, worst pain). Patients who requested analgesics were given flurbiprofen axetil 50 mg IV before they drank fluid, and/or oral loxoprofen sodium 60 mg with teprenone 50 mg after they drank. Patients who requested antiemetics were given metoclopramide 10 mg IV initially, and, if that was not effective, droperidol 0.5-1 mg IV before IV line removal, and/or a domperidone suppository 60 mg, given after IV line removal.

All patients were transferred to the overnight recovery area in the inpatient ward from the SRA in the DSU by 5:00 pm, after an observation period of more than 2.5h in the PACU/SRA. All patients were given oral loxoprofen sodium 60 mg, teprenone 50 mg, and cefcapene pivoxil 100 mg every 8h. A trained DSU nurse met directly with each patient in the morning on the day after surgery. Patients were asked about symptoms after DSU discharge, including PONV and the pain VAS, and the patients provided a score for the resumption of normal activities (RNA), scored as 0–10 (0, no activity; 10, back to normal daily activity), and answered questions about the acceptability of the 23-h admission procedure, in regard to future operations (choice between outpatient and inpatient procedures), using a standardized questionnaire [19].

In the study, values are expressed as medians (25th–75th percentiles). Statistical analyses were performed using the Mann-Whitney U-test. Differences at P < 0.05 were considered statistically significant.

Results

There were no significant differences in preoperative patient characteristics, durations of operation and anesthesia, intraoperative blood loss, or IV fluid volume between the two groups (Table 1). There were significant differences in the frequencies of intraoperative hypertension (systolic blood pressure >180 mmHg, 0 and 19% in groups SF and S, respectively), and nicardipine use (0 and 15%). The intraoperative heart rate and systolic blood pressure in group SF were significantly lower than those in group S (Table 2). Intraoperative ET $_{\rm CO_2}$ was higher and spontaneous respiratory rate and ET $_{\rm SEV}$ were lower in group SF than in group S (Table 3). One patient in group SF vomited just after LMA removal.

During the PACU/SRA stay, systolic blood pressure was slightly but significantly lower in group SF than in group S (Table 2). The incidences of nausea and vomit-

ing and the use of antiemetic drugs were significantly higher and IV fluid volume was larger in group SF (Table 4). Fewer patients in group SF drank fluid. The VAS scoring for pain was similar in both groups, but more patients in group SF required pain relief drugs (NSAIDs) more than 120min after PACU admission. No patient was given an opioid analgesic, as a rescue analgesic, after the operation. The times from PACU admission until the patients walked, voided, and were discharged from the SRA were significantly longer in group SF.

At the 24-h postoperative interview, more patients in group SF reported nausea during the overnight recovery area stay (Table 5). Fewer patients in group SF reported sore throat. The acceptability of the outpatient-basis procedure was slightly lower in group SF (68%) than in group S (85%), although the patient self-rated RNA score was not different between the two groups. All patients in group S returned home on postoperative day 1, but four patients (16%) in group SF required admission for more than 24h. The reasons for this longer stay were obvious persistent PONV in two patients, and patients' requests, due to anxiety, in the other two patients.

Table 1. Patients' preoperative characteristics and profiles in the operation room

Group	SF $(n = 25)$	S(n = 26)	Mann-Whitney U-test
Age (years)	55 (49–62)	57 (51–65)	NS
Height (cm)	156 (151–159)	154 (150–160)	NS
Body weight (kg)	54 (50–58)	53 (48–62)	NS
Body mass index (kg/m ²)	23 (21–24)	22 (21–25)	NS
ASA PS I/II (n)	17/8	18/8	NS
History			
Hypertension (n)	2	3	NS
Previous $PONV(n)$	2 2	3 5	NS
Motion sickness (n)	3	2	NS
Smoking (<i>n</i>)	1	1	NS
Menopause (n)	16	18	NS
Duration of operation (min)	106 (89–130)	135 (99–154)	NS
Duration of anesthesia (min)	150 (130–170)	180 (142–190)	NS
Intraoperative blood loss (ml)	70 (40–85)	70 (32–94)	NS
Intravenous fluid volume (ml) ^a	700 (650–800)	700 (563–813)	NS
Intraoperative cardiovascular episodes			
Tachycardia (n) ^b	1	4	NS
Bradycardia (n) ^c	2	1	NS
Hypertension $(n)^d$	0	5	P < 0.05
Hypotension $(n)^e$	0	0	NS
Drugs used in operation room			
Nicardipine (<i>n</i>)	0	4	P < 0.05
Metoclopramide (n)	1 ^f	0	NS
. r · · · · · · · · · · · ·		**	

Values are medians (25th–75th percentiles) or numbers (n)

PONV, postoperative nausea and vomiting

^a Intravenous volume in the preoperative preparation room plus volume in the operation room

bHeart rate >100 bpm lasting >5 min

^cHeart rate <50 bpm lasting >5 min

^dSystolic blood pressure >180 mmHg

^eSystolic blood pressure <70 mmHg

^fFor vomiting just after laryngeal mask airway removal

Table 2. Perioperative heart rate and systolic blood pressure values

Group	SF $(n = 25)$	S $(n = 26)$	Mann-Whitney U-test
Heart rate (bpm)			
Before induction of anesthesia	78 (68–83)	82 (72–91)	NS
Before starting the operation	65 (60–71)	72 (65–81)	P < 0.05
15 min after starting the operation	64 (59–72)	88 (80–97)	P < 0.01
30 min after starting the operation	64 (58–72)	83 (74–96)	P < 0.01
60 min after starting the operation	64 (62–72)	83 (73–90)	P < 0.01
After LMA removal	78 (75–88)	92 (82–104)	P < 0.05
At PACU admission	73 (65–77)	79 (71–92)	NS
0.5 h after PACU admission	72 (65–77)	76 (64–82)	NS
1h after PACU admission	68 (65–76)	74 (66–84)	NS
2h after PACU admission	72 (66–78)	76 (71–84)	NS
At discharge from SRA	73 (66–76)	76 (72–86)	NS
Systolic blood pressure (mmHg)			
Before induction of anesthesia	135 (116–150)	145 (130–163)	NS
Before starting the operation	93 (88–98)	102 (94–105)	P < 0.01
15 min after starting the operation	101 (93–112)	124 (111–136)	P < 0.01
30 min after starting the operation	106 (90–119)	122 (107–149)	P < 0.01
60 min after starting the operation	101 (95–120)	123 (108–137)	P < 0.05
After LMA removal	126 (117–148)	145 (132–156)	P < 0.05
At PACU admission	122 (113–135)	132 (122–148)	NS
0.5 h after PACU admission	122 (111–134)	134 (126–143)	P < 0.05
1h after PACU admission	120 (110–130)	127 (123–145)	P < 0.05
2h after PACU admission	119 (108–128)	130 (112–141)	P < 0.05
At discharge from SRA	120 (102–132)	122 (115–137)	NS

Values are medians (25th-75th percentiles)

LMA, laryngeal mask airway; PACU, postanesthesia care unit; SRA, stepdown recovery area

Table 3. Changes in respiration and sevoflurane concentrations during anesthesia

Group	SF $(n = 25)$	S(n = 26)	Mann-Whitney <i>U</i> -test
S _{PO2} (%)			
Before starting the operation	99 (98–100)	99 (98–100)	NS
15 min after starting the operation	99 (98–100)	99 (98–100)	NS
30 min after starting the operation	100 (99–100)	99 (98–100)	NS
60 min after starting the operation	99 (99–100)	99 (97–99)	NS
ET_{CO_2} (mmHg)			
Before starting the operation	45 (42–50)	46 (43–49)	NS
15 min after starting the operation	42 (39–49)	39 (36–43)	P < 0.05
30 min after starting the operation	43 (38–47)	38 (35–39)	P < 0.01
60 min after starting the operation	42 (38–48)	40 (36–43)	NS
Spontaneous respiratory rate (/min)			
Before starting the operation	18 (16–20)	20 (18–25)	P < 0.05
15 min after starting the operation	14 (10–17)	28 (25–31)	P < 0.01
30 min after starting the operation	14 (11–18)	27 (25–30)	P < 0.01
60 min after starting the operation	14 (11–18)	28 (23–32)	P < 0.01
$\mathrm{ET}_{\mathrm{SEV}}\left(\%\right)$			
Before starting the operation	2.2 (1.9–2.4)	2.3 (1.8–2.5)	NS
15 min after starting the operation	2.2 (2.0–2.4)	2.8 (2.4–3.4)	P < 0.01
30 min after starting the operation	2.2 (1.9–2.5)	2.7 (2.4–2.9)	P < 0.01
60 min after starting the operation	2.0 (1.7–2.4)	2.5 (2.2–3.0)	P < 0.01

Values are medians (25th-75th percentiles)

 S_{PO_2} , arterial oxygen saturation measured by pulse oximetry; ET_{CO_2} , end-tidal carbon dioxide concentration; ET_{SEV} , end-tidal sevoflurane concentration

Table 4. Recovery profiles in the PACU and SRA

Group	SF $(n = 25)$	S $(n = 26)$	Mann-Whitney U-tes	
Nausea (n)	15	7	P < 0.05	
Vomiting (n)	8	2	P < 0.05	
VAS pain score (mm)				
0.5 h after PACU admission	12 (3–32)	32 (20–40)	NS	
1 h after PACU admission	29 (14–53)	27 (21–39)	NS	
2h after PACU admission	19 (7–30)	10 (3–16)	NS	
At discharge from SRA	9 (2–17)	6 (0–15)	NS	
Time from PACU admission to				
Drinking (min)	140 (100–170)	133 (101–140)	NS^a	
Ambulation (min)	195 (158–219)	141 (101–175)	$P < 0.01^{\rm b}$	
Voiding (min)	195 (170–227)	137 (105–188)	$P < 0.01^{\circ}$	
Discharge from SRA (min)	272 (225–290)	237 (218–251)	P < 0.01	
Patients who did not				
Drink (n)	4	0	P < 0.05	
Walk (n)	2	0	NS	
Void (n)	4	1	NS	
Take a light meal (n)	21	18	NS	
IV volume in the PACU/SRA (ml)	690 (470–800)	495 (400–580)	P < 0.01	
Drugs used in the PACU/SRA				
Antiemetic drug $(n)^d$	10	1	P < 0.01	
Analgesic drug $(n)^e$	12	3	P < 0.01	
Used <60 min after PACU admission	2	1	NS	
Used 60-120 min after PACU admission	3	1	NS	
Used >120 min after PACU admission	7	1	P < 0.05	
Nicardipine (n)	0	1	NS	
Verapamil (n)	0	1	NS	
Ephedrine (n)	2	0	NS	

Values are medians (25th–75th percentiles) or numbers (n)

During the first 24-h postoperative period, the incidences of nausea (68% and 27%) and vomiting (32% and 8%) and the need for antiemetic medication (44% and 4%) were significantly higher in group SF than in group S.

Discussion

The present study demonstrated that the omission of fentanyl during sevoflurane anesthesia, combined with the administration of diclofenac suppository and lidocaine infiltration, decreased PONV incidence, expedited postanesthesia recovery, and increased patient acceptability of the 23-h admission procedure in female patients undergoing major breast cancer surgery.

It has been recognized that major breast surgery is associated with a high incidence of PONV [1–16,18,21], and PONV is the major limiting factor for performing such surgery as a day procedure [11,21]. The incidence of nausea during the first 24 postoperative hours in

group SF (68%) was almost comparable with that in previous reports of anesthesia without the use of prophylactic antiemetics (33%-85%) in major breast surgery [1–14]. Many factors are thought to be involved in the high incidence of PONV [18,21]. In the present study, factors thought to affect the incidence of PONV (such as female sex; age; body mass index; histories of motion sickness, smoking, and PONV; surgical procedure; duration of surgery; hydration; and intraoperative blood loss and pain intensity) were not different between the two groups, and perioperative management was standardized. Considering the well-recognized nauseant and emetic effects of opioids [18,20-23], fentanyl was the major factor accounting for the increased incidence of PONV in group SF, although it is undeniable that other factors in group SF, such as relative hypoventilation, hypercapnia, and low blood pressure may have been involved.

Some reports have shown that the prophylactic use of antiemetic drugs, such as metoclopramide (PONV incidence, 75% without prophylactic antiemetic and 55%

PACU, postanesthesia care unit; SRA, stepdown recovery area; VAS, visual analogue scale

^a Patients who did not drink fluid were not included in the statistics

^bPatients who did not walk were not included in the statistics

^cPatients who did not void were not included in the statistics

^dMetoclopramide, droperidol, and/or domperidone

^eFlurbiprofen axetil and/or loxoprofen

Table 5. Postoperative interview 24h after operation

Group	SF $(n = 25)$	S $(n = 26)$	Mann-Whitney U-test
Symptom after DSU discharge			
Nausea (n)	7	1	P < 0.05
Vomiting (n)	2	0	NS
Incision pain (n)	13	10	NS
Muscle pain (n)	5	4	NS
Sore throat (n)	9	18	P < 0.05
Hoarseness (n)	3	3	NS
Drowsiness (n)	12	7	NS
General malaise (n)	9	5	NS
Fever (n)	6	8	NS
Appetite loss (n)	7	3	NS
Headache (n)	6	4	NS
Sleeplessness (n)	4	10	NS
Dizziness (n)	4	2	NS
Urination disorder (n)	0	0	NS
Bleeding (n)	0	0	NS
Antiemetic medication $(n)^a$	3	0	NS
VAS pain score (mm)	9 (5–33)	6 (0–15)	NS
RNA scoreb	7 (6–8.5)	8 (7–8.5)	NS
Acceptability (n) ^c	17	22	P < 0.05

Values are numbers (n) or medians (25th-75th percentiles)

with prophylaxis) [13], dexamethazone (PONV incidence, 75% and 40%) [13], dolasetron (PONV incidence, 75% and 45%) [13], and ondansetron (PONV incidences 82% and 33% [4]; and 33% and 10% [9]) is effective in decreasing PONV in female patients undergoing major breast surgery in which a volatile anesthetic and an opioid analgesic are used. Our study suggests that the omission of fentanyl has a benefit similar to that of using the above antiemetics in reducing PONV frequencies in sevoflurane anesthesia in patients with major breast surgery. But others have reported that ondansetron (PONV incidence, 61% and 45%) [7], droperidol (PONV incidences, 50% and 37% [3]; and 61% and 48% [7]) and metoclopramide (PONV incidence, 50% and 43%) [3] were not necessarily effective in breast surgery. Pharmacological prophylaxis may increase costs and predispose to adverse events [6,21]. Further studies are required to compare the advantages and disadvantages of antiemetic prophylaxis and the omission of intraoperative opioid use in major breast surgery.

In our study, the PONV incidences after PACU/SRA discharge (late PONV; 28% and 4% in groups SF and S, respectively) were lower than that during the PACU/SRA stay (early PONV; 60% and 27%). Many studies have demonstrated that the incidence of late PONV was higher (or not lower) than that of early PONV in breast surgery with or without antiemetic prophylaxis

[1–3,7,9]. In the earlier reports, patients were given opioids after PACU discharge, but no patient in our study received opioids postoperatively. Volatile anesthetics are assumed to be the major cause of early PONV but not late PONV [21,24]. The high incidence of late PONV in the previous studies was probably due to postoperative opioid use. Because the emetic effect of opioids is markedly enhanced by vestibular stimulation, and opioids increase vestibular sensitivity [23], ambulation under the influence of opioids could increase the risk of nausea and vomiting.

The weak point of fentanyl-free sevoflurane anesthesia could be intraoperative hemodynamic instability. The increased heart rate and blood pressure during surgery in our group S may reflect inadequate intraoperative analgesia. Local infiltration anesthesia performed by the surgeons was probably insufficient to block the noxious surgical stimuli completely in some of our patients. Opioid analgesics can attenuate the hemodynamic response to noxious surgical stimuli [22], but with sevoflurane, it is difficult to attenuate this response, because the noxious stimulation-induced sympathetic response is inversely proportional to the sevoflurane dose [25]. Because intraoperative tachycardia and hypertension are associated with perioperative myocardial ischemia, they should be treated. To decrease the risk of intraoperative hypertension and tachycardia during fentanyl-free sevoflurane anesthesia, a beta-blocker,

VAS, visual analogue scale

^aMetoclopramide 5 mg PO

^bScore for patient's self-assessment of resumption of normal activity (0–10; score 0, no activity; 10, back to normal activity)

^cAcceptance of 23-h admission procedure in future, number of "yes" answers

alpha 2 agonist, more extensive local infiltration anesthesia, or epidural or paravertebral block may be worth considering [16,18].

Same-day or 23-h admission surgery is unpopular in Japan, and patients can choose inpatient surgery without great difficulty in our hospital. Our results in this study, especially patient acceptability and patient request for hospital admission, were influenced, presumably, by the difficult social situations for ambulatory surgery and the readily available inpatient beds in our hospital. In spite of the hard circumstances, 85% of patients in group S stated that they would accept the same kind of procedure in future, and no patient in group S required admission for more than 24h. Because an acceptance rate of 85% is not satisfactory, there may be more room for improvement with our care.

Our study suggests that intensive postoperative analgesia is not necessary after major breast cancer surgery with sevoflurane anesthesia and the intraoperative application of an NSAID and local infiltration anesthesia. More patients in group SF than in group S required analgesic drugs more than 120 min after PACU admission. The exact reason for this is not clear. It may be associated with the longer bed-rest time and delayed discharge in group SF.

In conclusion, the present study demonstrates that the omission of fentanyl during sevoflurane anesthesia, combined with local infiltration anesthesia and an NSAID, leads to relatively unstable intraoperative cardiovascular responses, but decreases PONV incidence and accelerates postanesthesia recovery in female patients undergoing major breast cancer surgery, compared with sevoflurane-fentanyl anesthesia. The result suggests that sevoflurane-fentanyl anesthesia without adequate antiemetic prophylaxis may not be suitable for ambulatory breast cancer surgery. Further studies are necessary to decrease the incidences of PONV, pain, and perioperative hemodynamic instability, and to facilitate postanesthesia recovery in patients with major breast surgery.

Acknowledgments. We wish to thank Atsuko Yamaguchi, R.N., and Akiko Eto, R.N., and the nursing staff in the DSU, Kyoto University Hospital, for data entry, and Dr. Hironori Kato, Second Division, Department of Surgery, Kyoto University Hospital, and Professor Takashi Inamoto, Department of Nursing, School of Health Sciences, Kyoto University, for their helpful cooperation. This research was supported in part by Grants-in-Aid for Scientific Research from the Japanese Ministry of Education, Science, Sports, and Culture (nos. 14571432 and 17591627).

References

 Oddby-Muhrbeck E, Jakobsson J, Andersson L, Askergren J (1994) Postoperative nausea and vomiting. A comparison be-

- tween intravenous and inhalation anaesthesia in breast surgery. Acta Anaesthesiol Scand 38:52-56
- Gan TJ, Ginsberg B, Grant AP, Glass PSA (1996) Double-blind, randomized comparison of ondansetron and intraoperative propofol to prevent postoperative nausea and vomiting. Anesthesiology 85:1036–1042
- 3. Fujii Y, Tanaka H, Toyooka H (1998) Prevention of nausea and vomiting in female patients undergoing breast surgery: a comparison with granisetron, droperidol, metoclopramide and placebo. Acta Anaesthesiol Scand 42:220–224
- Sadhasivam S, Saxena A, Kathirvel, Kannan TR, Trikha A, Mohan V (1999) The safety and efficacy of prophylactic ondansetron in patients undergoing modified radical mastectomy. Anesth Analg 89:1340–1345
- Vanacker BF (1999) The impact of nitrous oxide on postoperative nausea and vomiting after desflurane anesthesia for breast surgery. Acta Anaesthsiol Belg 50:77–81
- Jaffe SM, Campbell P, Bellman M, Baildam A (2000) Postoperative nausea and vomiting in women following breast surgery: an audit. Eur J Anaesth 17:261–264
- Reihnér E, Grunditz R, Giesecke K, Gustafsson LL (2000) Postoperative nausea and vomiting after breast surgery: efficacy of prophylactic ondansetron and droperidol in a randomized placebo-controlled study. Eur J Anaesthesiol 17:197–203
- Karlsen KL, Persson E, Wennberg E, Stenqvist O (2000) Anesthesia, recovery and postoperative nausea and vomiting after breast surgery. A comparison between desflurane, sevoflurane and isoflurane anaesthesia. Acta Anaesthesiol Scand 44:489–493
- Jokela RM, Kangas-Saarela TA, Valanne JVI, Koivuranta MK, Ranta PO, Alahuhta SM (2000) Postoperative nausea and vomiting after sevoflurane with or without ondansetron compared with propofol in female patients undergoing breast surgery. Anesth Analg 91:1062–1065
- Johansson A, Axeleson J, Ingvar C, Luttropp H-H, Lundberg J (2000) Preoperative ropivacaine infiltration in breast surgery. Acta Anaesthesiol Scand 44:1093–1098
- Choi HK, Chow LWC, Goh LC, Tsui SL, Lee FCW (2001) The impact of postoperative nausea and vomiting on the practice of day surgery for Chinese women with breast diseases. Ambul Surg 9:29–32
- Oddby-Muhrbeck E, Eksborg S, Bergendahl HTG, Muhrbeck O, Lönnqvist PA (2002) Effects of clonidine on postoperative nausea and vomiting in breast cancer surgery. Anesthesiology 96:1109– 1114
- Zeid HA, Al-Gahamdi A, Abdul-Hadi M (2002) Dolasetron decreases postoperative nausea and vomiting after breast surgery. Breast J 8:216–221
- Purhonen S, Niskanen M, Wüstefeld M, Mustonen P, Hynynen M (2003) Supplemental oxygen for prevention of nausea and vomiting after breast surgery. Br J Anaesth 91:284–287
- Margolese RG, Lasry J-CM (2000) Ambulatory surgery for breast cancer patients. Ann Surg Oncol 7:181–187
- Dooley WC (2002) Ambulatory mastectomy. Am J Surg 184;545– 549
- Marchal F, Dravet F, Classe JM, Campion L, François T, Labbe D, Robard S, Théard JL, Pioud R (2005) Post-operative care and patient satisfaction after ambulatory surgery for breast cancer patients. Eur J Surg Oncol 31:495–499
- White PF, Freire AR (2005) Ambulatory (outpatient) anesthesia.
 In: Miller RD (ed) Miller's anesthesia, 6th edn. Elsevier Churchill Livingston, Philadelphia, pp 2589–2635
- Shirakami G, Teratani Y, Namba T, Hirakata H, Tazuke-Nishimura M, Fukuda K (2005) Delayed discharge and acceptability of ambulatory surgery in adult outpatients receiving general anesthesia. J Anesth 19:93–101
- White PF (2002) The role of non-opioid analysesic techniques in the management of pain after ambulatory surgery. Anesth Analg 94:577–585

- 21. Gan TJ, Meyer T, Apfel CC, Chung F, Davis PJ, Eubanks S, Kovac A, Philip BK, Sessler DI, Temo J, Tramèr MR, Watcha M (2003) Consensus guidelines for managing postoperative nausea and vomiting. Anesth Analg 97:62–71
- Fukuda K (2005) Intravenous opioid anesthetics. In: Miller RD (ed) Miller's anesthesia, 6th edn. Elsevier Churchill Livingston, Philadelphia, pp 379–437
- Gutstein HB, Akil H (2001) Opioid analgesics. In: Hardman JG, Limbird LE (eds) Goodman and Gilman's the pharmacological basis of therapeutics, 10th edn. McGraw-Hill, New York, pp 569– 619
- 24. Apfel CC, Kranke P, Katz MH, Goepfert C, Papenfuss T, Rauch S, Heineck R, Greim C-A, Roewer N (2002) Volatile anesthetics may be the main cause of early but not delayed postoperative vomiting: a randomized controlled trial of factorial design. Br J Anaesth 88:659–668
- Segawa H, Mori K, Murakawa M, Kasai K, Shirakami G, Adachi T, Arai T (1998) Isoflurane and sevoflurane augment norepinephirine responses to surgical noxious stimulation in humans. Anesthesiology 89:1407–1413