

Comparison of Recovery Characteristics, Postoperative Nausea and Vomiting, and Gastrointestinal Motility With Total Intravenous Anesthesia With Propofol Versus Inhalation Anesthesia With Desflurane for Laparoscopic Cholecystectomy: A Randomized Controlled Study

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ABSTRACT

BACKGROUND: Clinical effects, recovery characteristics, and costs of total intravenous anesthesia with different inhalational anesthetics have been investigated and compared; however, there are no reported clinical studies focusing on the effects of anesthesia with propofol and desflurane in patients undergoing laparoscopic cholecystectomy.

OBJECTIVE: The aim of this study was to determine the effects of total intravenous anesthesia with propofol and alfentanil compared with those of desflurane and alfentanil on recovery characteristics, postoperative nausea and vomiting (PONV), duration of hospitalization, and gastrointestinal motility.

METHODS: Patients classified as American Society of Anesthesiologists physical status I or II undergoing elective laparoscopic cholecystectomy due to benign gallbladder disease were enrolled in the study. Patients were randomly assigned at a 1:1 ratio to receive total intravenous anesthesia with propofol (2–2.5 mg/kg) and alfentanil (20 µg/kg) or desflurane (4%–6%) and alfentanil (20 µg/kg). Perioperative management during premedication, intraoperative analgesia, relaxation, ventilation, and postoperative analgesia were carried out identically in the 2 groups. Extubation time, recovery time, PONV, postoperative antiemetic requirement, time to gastrointestinal motility and flatus, duration of hospitalization, and adverse effects were recorded. Postoperative pain was assessed using a visual analogue scale.

RESULTS: Sixty-eight patients were assessed for inclusion in the study; 5 were excluded because they chose open surgery and 3 did not complete the study because they left the hospital. Sixty patients (33 women, 27 men) completed the study. Recovery time was significantly shorter in the propofol group (n = 30) compared with the desflurane group (n = 30) (8.0 [0.77] vs 9.2 [0.66] min, respectively; *P* < 0.005).

Fifteen patients (50.0%) in the propofol group and 20 patients (66.7%) in the desflurane group experienced nausea during the first 24 hours after surgery. The difference was not considered significant. In the propofol group, significantly fewer patients had vomiting episodes compared with those in the desflurane group (2 [6.7%] vs 16 [53.3%]; $P < 0.005$). Significantly fewer patients in the propofol group required analgesic medication in the first 24 hours after surgery compared with those in the desflurane group (10 [33.3%] vs 15 [50.0%]; $P < 0.005$). Patients in the propofol group experienced bowel movements in a significantly shorter period of time compared with patients in the desflurane group (8.30 [1.67] vs 9.76 [1.88] hours; $P = 0.02$). The mean time to flatus occurred significantly sooner after surgery in the propofol group than in the desflurane group (8.70 [1.79] vs 9.46 [2.09] hours; $P = 0.01$). The duration of hospitalization after surgery was significantly shorter in the propofol group than in the desflurane group (40.60 [3.49] vs 43.60 [3.56] hours; $P = 0.03$).

CONCLUSION: Total intravenous anesthesia with propofol and alfentanil was associated with a significantly reduced rate of PONV and analgesic consumption, shortened recovery time and duration of hospitalization, accelerated onset of bowel movements, and increased patient satisfaction compared with desflurane and alfentanil in these patients undergoing laparoscopic surgery who completed the study. (*Curr Ther Res Clin Exp.* 2009;70:94–103) © 2009 Excerpta Medica Inc.

KEY WORDS: total intravenous anesthesia, propofol, desflurane, alfentanil, laparoscopic cholecystectomy.

INTRODUCTION

Laparoscopic cholecystectomy is usually associated with a short period of hospitalization; however, postoperative nausea and vomiting (PONV) and the late onset of bowel movements are the most common reasons for prolonged hospitalization, especially after laparoscopic surgeries.^{1–3} Patient satisfaction is reduced because of these factors.

Anesthetic techniques that reduce these adverse effects (AEs) are essential for laparoscopic interventions. Total intravenous anesthesia with propofol and alfentanil is increasingly used in same-day surgery because of its suggested beneficial effects on recovery time, PONV, and pain.^{1,3} Six studies have indicated that propofol and alfentanil were associated with reduced PONV, duration of hospitalization, and recovery time^{1–6}; however, most of the data were obtained from studies performed on nonselected patients. The few studies of patients undergoing laparoscopic surgery suggested that propofol and alfentanil had no significant effects on gastrointestinal motility in the postoperative period.^{1,7,8} Factors other than the type of anesthesia may affect motility after laparoscopic cholecystectomy.^{3,5,6} A meta-analysis found that there was insufficient evidence to conclude that propofol and alfentanil reduced PONV.^{8–11}

This study was conducted to investigate the effects of propofol and alfentanil total intravenous anesthesia on PONV, recovery time, gastrointestinal motility, patient satisfaction, and duration of hospitalization after laparoscopic cholecystectomy compared with the outcomes of patients administered desflurane and alfentanil anesthesia.

PATIENTS AND METHODS

This study was approved by the Ethics Committee of Mustafa Kemal University, Antakya, Hatay, Turkey. Patients provided written informed consent before participating in the study.

All patients, classified by the American Society of Anesthesiologists as physical status I or II,¹² undergoing elective laparoscopic cholecystectomy due to benign gallbladder disease were assessed for inclusion in the study. Patients were recruited for enrollment preoperatively on the day of surgery.

Exclusion criteria were allergy to any of the medications used in the study, current symptoms of nausea or vomiting, or treatment with an antiemetic drug. Patients who chose open cholecystectomy were also excluded.

Demographic data, including age, weight, and history of PONV or motion sickness, were recorded. Patients were randomized into 2 groups using a computer-generated block-randomized number table. Randomization was performed by a statistical expert who was blinded to the study design.

All patients were premedicated with IV midazolam 2 mg, 30 minutes before the induction of anesthesia. In the operating room, patients underwent routine monitoring, including blood pressure (BP), heart muscle electrical potential, oxygen saturation, and end-tidal carbon dioxide. To reduce the pain associated with propofol infusion, patients received IV 1% lidocaine 0.5 mg/kg.

In the propofol group, anesthesia was induced with IV alfentanil 20 µg/kg and then propofol at 2 to 2.5 mg/kg was administered. To maintain anesthesia, propofol was initiated at 10 mg/kg/h and was reduced by 2 mg/kg/h every 10 minutes to 6 mg/kg/h at which time alfentanil 0.5 µg/kg/min was administered with an intravenous infusion pump (Injectomat Agilia, Fresenius Kabi AG, Bad Homburg, Germany). In the group receiving desflurane, anesthesia was induced with propofol 2 to 2.5 mg/kg and alfentanil 20 µg/kg and maintained with desflurane 4% to 6% and IV alfentanil 0.5 µg/kg/min. To avoid the possible effects of lidocaine on the findings, we administered lidocaine to both groups. After sufficient anesthesia was achieved, muscle relaxation was achieved with IV rocuronium bromide 0.6 mg/kg. Endotracheal intubation was performed after 90 seconds in both groups. Both groups were mechanically ventilated with 30% oxygen in air. End-tidal carbon dioxide was maintained between 35 to 40 mm Hg in both groups. The depth of anesthesia was measured using the bispectral index score,⁴ and anesthesia was adjusted to obtain a score of 40 to 60 in both groups. Preoperative analgesia was provided with alfentanil infusion (0.5 µg/kg/min) and was stopped 30 minutes before the end of the procedure. Antiemetic prophylaxis was not administered to any patient. For each patient, a nasogastric tube was in place during anesthesia. At the end of surgery, anesthetic agents were stopped and neuromuscular blockade was reversed with IV neostigmine 1.5 mg and atropine 0.5 mg. The time of discontinuation of the anesthetic agents and the extubation time were recorded. The time at which each patient responded to verbal commands (*recovery time*) was recorded.

Postoperative analgesia was initially provided with titrated IM pethidine 5 mg/kg. Diclofenac sodium 75 mg was administered intramuscularly if the visual analog scale

(VAS) score for pain was >5 . VAS was assessed with a 10-cm scale (0 = no pain to 10 = unbearable pain). Total analgesic consumption was recorded for each patient. If PONV occurred, patients were administered orally prochlorperazine 10 mg.

Patients were blinded to randomization and staff in the postanesthesia care unit collecting the data were blinded to the study protocol. One anesthesiologist (Z.A.) provided anesthesia and another anesthesiologist, who was blinded, recorded the data after the induction of anesthesia.

The duration of hospitalization, pain score, and number of PONV episodes requiring antiemetic treatment until the time of recovery were recorded. Assessments were recorded 15 minutes and 2, 6, 12, 24, 36, and 48 hours after surgery. Bowel movements were auscultated, and the time of flatus was recorded. Patients were initiated on an oral diet regimen after the onset of bowel movements.

Forty-eight hours after surgery, the discharged patients were interviewed by telephone and those who were still hospitalized were interviewed in the hospital to assess their satisfaction. Postdischarge nausea and vomiting were recorded. Postoperative nausea was recorded from the medical chart during the hospitalization process and after discharge through patient interview.

Satisfaction with the surgery as well as preoperative and postoperative anesthesia were assessed using a 3-point scale: 1 = not satisfied; 2 = satisfied; and 3 = completely satisfied.

AEs (eg, hypotension, allergic reactions, respiratory depression, agitation, or delirium) were recorded during surgery and hospitalization.

STATISTICAL ANALYSIS

We calculated that 20 patients per group were required to provide 80% power ($\beta = 0.2$) based on the intent to detect a reduction in the incidence of PONV, or the requirement for antiemetic treatment, from 60% with inhalational anesthesia with desflurane and alfentanil to 40% with propofol and alfentanil in the intent-to-treat population. The primary outcome was the incidence of *complete response*, defined as the absence of nausea and vomiting. The Mann-Whitney and χ^2 tests were used for statistical analysis. $P < 0.05$ was considered statistically significant. Data were expressed as mean (SD). Statistical analyses were calculated using SPSS version 13.0 (SPSS Inc., Chicago, Illinois).

RESULTS

Sixty-eight patients were assessed for inclusion in the study; 3 were excluded because they chose open surgery and 5 did not complete the study because they left the hospital in the first 12 hours postsurgery ($n = 2$, propofol group) or on day 1 for personal reasons (lack of insurance [$n = 2$], desflurane group; death in the family [$n = 1$], desflurane group). Therefore, 60 patients (33 women, 27 men) completed the study (Table I). There were no significant differences in patient characteristics, perioperative management, or postoperative pain management between the propofol ($n = 30$) and the desflurane ($n = 30$) groups. Surgery and anesthesia administration were uneventful in all patients.

Table I. Demographic and clinical characteristics of the study patients (N = 60).*

Characteristic	Propofol Group (n = 30)	Desflurane Group (n = 30)
Age, mean (SD), y	55.1 (8.8)	56.2 (12.6)
Sex, no. (%)		
Female	17 (56.7)	16 (53.3)
Male	13 (43.3)	14 (46.7)
Weight, mean (SD), kg	72.1 (5.9)	72.0 (9.7)
ASA I/II	18/12	20/10
Operating time, mean (SD), min	78.4 (7.1)	80.7 (10.0)
Anesthesia time, mean (SD), min	91.3 (5.5)	91.0 (9.3)

ASA = American Society of Anesthesiologists.

*No significant between-group differences were found.

Mean (SD) operating time and mean anesthesia time did not differ significantly between the 2 groups (Table I). Mean arterial BP was not significantly different; 101.40 mm Hg (systolic/diastolic, 129/82 mm Hg) in the propofol group and 109.70 mm Hg (126/94 mm Hg) in the desflurane group. *Hypotension* (defined as BP <90/60 mm Hg) occurred in significantly more patients in the propofol group than in the desflurane group (8 vs 1, respectively; $P < 0.005$). Three patients with hypotension in the propofol group received IV ephedrine 5 mg.

Mean time to extubation was significantly shorter in the propofol group than the desflurane group (6.40 [4.20] vs 7.60 [0.68] min, respectively; $P < 0.05$). Recovery time was significantly shorter in the propofol group than the desflurane group (8.00 [0.77] vs 9.20 [0.66] min; $P < 0.05$) (Table II).

Fifteen patients (50.0%) in the propofol group and 20 patients (66.7%) in the desflurane group had nausea during the first 24 hours after surgery, although the difference was not significant. The number of patients who required antiemetic treatment in the first 24 hours after surgery was similar in the propofol group and the desflurane group (12 [40.0%] vs 16 [53.3%], respectively). Significantly fewer patients in the propofol group had vomiting episodes than in the desflurane group (2 [6.7%] vs 16 [53.3%]; $P < 0.005$). Significantly fewer patients in the propofol group required analgesic medication in the first 24 hours after surgery than in the desflurane group (10 [33.3%] vs 15 [50.0%]; $P < 0.005$).

The mean (SD) VAS score for pain in the propofol group was significantly lower at 15 minutes compared with the desflurane group (2.96 [0.71] vs 4.63 [1.03] min, respectively; $P = 0.01$) and at 1 hour after surgery (4.13 [1.50] vs 5.70 [0.67]; $P < 0.01$). Two patients (6.7%) in the propofol group and 8 patients (26.7%) in the desflurane group required analgesic treatment as rescue medication during the first 6 hours after surgery. After 6 hours, none of the patients in either group required antiemetic medication or analgesic treatment.

Patients in the propofol group had bowel movements significantly earlier than patients in the desflurane group (8.30 [1.67] vs 9.76 [1.88] hours, respectively; $P =$

Table II. Recovery characteristics by treatment group in these patients receiving total intravenous anesthesia with propofol versus inhalation anesthesia with desflurane for laparoscopic cholecystectomy (N = 60). Data are mean (SD).

Characteristic	Propofol Group (n = 30)	Desflurane Group (n = 30)
Time to extubation, min*	6.40 (4.20)	7.60 (0.68)
Recovery time, min*	8.00 (0.77)	9.20 (0.66)
Pain VAS [†] at 15 min [‡]	2.96 (0.71)	4.63 (1.03)
Pain VAS [†] at 60 min [§]	4.13 (1.50)	5.70 (0.67)

VAS = visual analog scale.

* $P < 0.05$.

[†]Scale: 0 = no pain to 10 = unbearable pain.

[‡] $P = 0.01$.

[§] $P < 0.01$.

0.02); therefore, an oral diet was resumed earlier in the propofol group. Flatus occurred significantly sooner after surgery in the propofol group compared with the desflurane group (8.70 [1.79] vs 9.46 [2.09] hours; $P = 0.01$). The duration of hospitalization after surgery was significantly shorter in the propofol group than in the desflurane group (40.60 [3.49] vs 43.60 [3.56] hours; $P = 0.03$) (Table III). No patient in either group remained hospitalized >48 hours after surgery because of prolonged nausea and vomiting. One patient (3.3%) in the propofol group and 3 patients (10.0%) in the desflurane group were readmitted to the hospital because of nausea.

One patient (3.3%) in the propofol group and 4 patients (13.3%) in the desflurane group were not satisfied with the surgery ($P < 0.001$). Twenty-two patients (73.3%) in the propofol group and 26 patients (86.7%) in the desflurane group were satisfied with the surgery. Seven patients (23.3%) in the propofol group and none in the desflurane group were completely satisfied with the surgery ($P < 0.01$).

Table III. Time to the start of bowel movements, mobilization, and flatus, and duration of hospitalization after surgery in these patients receiving total intravenous anesthesia with propofol versus inhalation anesthesia with desflurane for laparoscopic cholecystectomy (N = 60). Data are mean (SD).

Characteristic	Propofol Group (n = 30)	Desflurane Group (n = 30)	<i>P</i>
Time to onset of bowel movements, h	8.30 (1.67)	9.76 (1.88)	0.02*
Time to mobilization, h	9.40 (1.79)	11.10 (2.02)	0.25
Time to flatus, h	8.70 (1.79)	9.46 (2.09)	0.01*
Duration of hospitalization, h	40.60 (3.49)	43.60 (3.56)	0.03*

* $P < 0.05$.

Respiratory depression or agitation was not reported by any of the patients. Although 2 patients had diarrhea on day 1 and 3 patients had rectal bleeding on day 2, no patients reported headache or lumbar pain.

DISCUSSION

The present study found that total intravenous anesthesia with propofol and alfentanil was associated with significantly reduced PONV and analgesic consumption, shortened recovery time and duration of hospitalization, and accelerated bowel movements in these patients undergoing laparoscopic surgery who completed the study when compared with anesthesia with desflurane and alfentanil. The rate of patient satisfaction was significantly higher in the propofol group than in the desflurane group.

During surgery, anesthesia was uneventful with both anesthetic techniques. However, systolic and diastolic BP were significantly more stable in the desflurane group. This finding is consistent with the findings of Ozkose et al¹³ and Smith and Thwaites.¹⁴ Hypotension after propofol anesthesia is an expected event and the incidence has been reported to be between 10% and 55%.^{13,15-17}

PONV has been the most common cause of prolonged hospitalization after same-day surgery, and is experienced in 30% to 50% of the cases, especially after laparoscopic cholecystectomy.¹ Unexpected readmission to the hospital because of uncontrolled PONV has led to substantial costs in terms of lost productivity for both patients and those caring for them.⁴ In the present study, significantly more patients in the desflurane group experienced PONV and required antiemetic drug treatment compared with the propofol group ($P < 0.001$). Paech et al¹ reported that propofol and alfentanil, with or without dolasetron, was associated with significantly reduced PONV compared with inhalation anesthesia with sevoflurane in patients undergoing gynecologic laparoscopy. Raeder et al,¹⁸ in a study comparing desflurane and propofol anesthesia in patients undergoing laparoscopic surgery, reported that propofol anesthesia was associated with significantly less postoperative nausea ($P < 0.001$). Similarly, Grundmann et al¹⁹ found that propofol resulted in significantly less postoperative analgesic consumption and nausea compared with desflurane. However, if propofol was substituted for volatile anesthetics, the risk for PONV was reduced by only ~20%.¹⁰ Visser et al²⁰ compared the effects of propofol with alfentanil and isoflurane with nitrous oxide anesthesia on PONV in unselected patients. It was reported that the propofol and alfentanil combination was associated with a clinically relevant reduction of PONV, and both anesthetic techniques were similar otherwise. Juckenhöfel et al²¹ investigated the effect of propofol and alfentanil, and balanced anesthesia with sevoflurane in laparoscopic surgery. No significant between-group difference in shivering or PONV was reported. In the present study, we compared desflurane anesthesia with propofol and alfentanil and found a significantly reduced incidence of PONV. Desflurane's AEs and pharmacologic characteristics are similar to those of isoflurane.

The delayed onset of bowel movements may cause patient discomfort and delayed discharge from the hospital. Walldén et al⁷ studied the effect of anesthetic technique on early postoperative gastric emptying using the acetaminophen method. Acetaminophen (paracetamol) is not absorbed from the stomach but is rapidly absorbed

from the small intestine; therefore, the rate of gastric emptying determines the rate of absorption of acetaminophen administered into the stomach. Acetaminophen 1.5 g was administered through a nasogastric tube, and blood samples were drawn during a 2-hour period. It was found that early gastric emptying with inhalation anesthesia was similar to that with propofol anesthesia. Gastric emptying was delayed in varying ranges with both anesthetic techniques. Liao et al²² investigated the effect of propofol and alfentanil anesthesia on gastrointestinal motility by measuring plasma motilin concentration after laparoscopic cholecystectomy and also did not find a significant influence of the anesthesia type on the recovery of intestinal motion. In the present study, we found that gastric motility recovered significantly earlier in the propofol group ($P < 0.001$). In contrast to previous studies, we used clinical assessment rather than laboratory methods to evaluate gastric motility. This may be the reason for the different findings.

The mean duration of hospitalization was significantly shorter and patient satisfaction was significantly higher in the propofol group than in the desflurane group (both, $P < 0.001$). The subjective degree of patient satisfaction and the rate of satisfied patients were significantly higher in the propofol group than the desflurane group. These findings are consistent with previous studies.^{3-7,13,14} Although the improvement in recovery time in the propofol group in contrast to the desflurane group may not be important clinically, we suggest that the other advantages (especially patient satisfaction) support the use of propofol and alfentanil in patients undergoing laparoscopic cholecystectomy.

Hypotension is a commonly expected AE associated with propofol and alfentanil; a variety of AEs, including convulsions, seizures, opisthotonos, involuntary muscle activities, and tonic-clonic movements, have been observed with propofol.^{19,21,22} Line infection due to intravenous catheterization is another complication.^{21,22} Propofol infusion syndrome involves severe metabolic acidosis, rhabdomyolysis, renal failure, and cardiac failure in association with prolonged propofol infusion, critical illness, and concurrent administration of catecholamines and steroids.²³ Although this condition is not expected with short-term infusion, caregivers should be aware of this possible complication because of the high mortality rate associated with it.

The major disadvantage of propofol and alfentanil, as reported in the current literature, is its cost.^{1,13,20,21,24,25} We did not assess the cost-effectiveness of propofol and alfentanil, which is a limitation of this study. Another limitation was the small size of the study groups. However, we believe that the lower consumption of antiemetic medications during hospitalization and in the postdischarge period, the shorter duration of hospitalization, and the lower rate of postdischarge readmission to the hospital in the propofol group should be considered benefits of propofol and alfentanil that help reduce the overall costs associated with laparoscopic cholecystectomy.

CONCLUSION

Total intravenous anesthesia with propofol and alfentanil was associated with significantly reduced PONV and analgesic consumption, shortened recovery time and duration of hospitalization, accelerated onset of bowel movements, and increased patient satis-

fraction without significant AEs compared with desflurane and alfentanil in these patients undergoing laparoscopic surgery who completed the study.

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