Propofol *versus* Thiamylal-Enflurane Anesthesia for Outpatient Laparoscopy

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Study Objective: *To determine whether propofol anesthesia differs from thiamylal-enflurane anesthesia in induction characteristics, intraoperative hemodynamics, postoperative side effects, and postoperative psychomotor function recovery.*
Design: *A randomized, double-blind, two-group study.*
Setting: *A large university hospital with gynecologic outpatient operations performed in an integrated operating room suite.*
Patients: *Sixty adult women (ASA physical status I or II) undergoing an outpatient gynecologic laparoscopic operation with an anesthesia time of approximately 60 minutes.*
Interventions: *No pharmacologic premedication. Pretreatment with intravenous droperidol 0.6 mg and sufentanil 0.2 μg/kg before induction of anesthesia. Anesthesia was induced with either thiamylal 4 mg/kg (Group 1) or propofol 2.5 mg/kg (Group 2). Anesthesia was maintained with either nitrous oxide (N_2O) and enflurane, 2-0.5% inspired concentrations; (Group 1) or with a continuous infusion of propofol 200-100 μg/kg/min and N_2O (Group 2).*
Measurements and Main Results: *In psychomotor function tests (Trieger dot test and p-deletion test) administered preoperatively and postoperatively, no difference was found between the groups. No difference was found in induction time, although significantly more patients reported pain after the propofol injection, or in intraoperative hemodynamics (mean arterial pressure and heart rate). Immediate recovery time (emergence from anesthesia) and intermediate recovery time (ambulation, oral intake, and discharge time) were significantly shorter after propofol anesthesia. Fewer postoperative side effects, such as nausea and vomiting, were reported after propofol anesthesia.*
Conclusions: *Induction and maintenance of anesthesia with propofol were comparable to those with thiamylal-enflurane, except patients experienced more pain on injection after propofol. Both immediate and intermediate recovery were more rapid after propofol anesthesia compared with enflurane-based anesthesia.*

Keywords: Inhaled anesthetic, enflurane; intravenous anesthetics, propofol, thiamylal; outpatient anesthesia, recovery.

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Introduction

The unprecedented growth of outpatient surgery in this country is challenging every anesthesiologist to provide anesthesia that minimizes recovery time and side effects. The pharmacokinetic profile of propofol, with its high clearance rate and short elimination half-life,[1] suggests that this drug may be helpful in meeting this challenge. Indeed, several studies have shown shortened emergence when comparing propofol with thiopental sodium as an

induction drug.[2,3] However, few studies have compared a maintenance infusion of propofol with an inhalation technique in a homogeneous outpatient surgical population where the frequency of postoperative side effects, especially nausea and vomiting, is known to be high.[4,5] This study compares the induction characteristics, intraoperative hemodynamics, and recovery characteristics of a thiamylal-enflurane anesthetic with a propofol-infusion anesthetic for outpatient laparoscopy.

Materials and Methods

Sixty nonpregnant female patients (ages 18 to 45 years; ASA physical status I or II) scheduled for outpatient laparoscopy were studied. The University of Michigan Medical Center's Institutional Human Use Review Board approved the study, and each patient gave written informed consent. Patients who were obese (>100 kg) or receiving central nervous system depressant medications, including opiates, during the 7 days prior to surgery were excluded. Patients were randomly assigned to receive either thiamylal-enflurane (Group 1, n = 30) or propofol-based anesthesia (Group 2, n = 30). One of the investigators was blinded to the anesthetic technique and performed all the preanesthetic and postanesthetic evaluations outside of the operating room.

In the preanesthetic holding room, we gave two baseline psychomotor function tests, the p-deletion test[6] and the Trieger dot test,[7] to each patient. We placed an 18-gauge intravenous (IV) cannula in the dorsum of the patient's hand. No premedication was used in any patient, but all patients received droperidol 0.6 mg IV and sufentanil 0.2 μg/kg IV 2 minutes prior to induction of anesthesia. Following denitrogenation, anesthesia in Group 1 was induced with thiamylal 4.0 mg/kg IV given over 30 seconds and vecuronium 0.1 mg/kg IV. Tracheal intubation was performed after ventilation of the lungs with 2% enflurane in oxygen (O_2) for 3 to 4 minutes. Nitrous oxide (N_2O) (65% to 70%) was added to the inspired gas mixture after tracheal intubation. The inspired concentration of enflurane was maintained at 2% for the first 15 minutes, decreased in a planned fashion to 1% for the next 15 minutes, and then decreased to 0.5% for the remainder of the operation.

Following denitrogenation, anesthesia was induced in Group 2 with propofol 2.5 mg/kg IV given over 30 seconds and vecuronium 0.1 mg/kg IV. A continuous infusion of propofol 200 μg/kg/min was started immediately after induction of anesthesia. Following tracheal intubation, anesthesia was maintained with a propofol infusion and N_2O (65% to 70%) in O_2. The maintenance infusion rate of propofol was reduced in a planned fashion from 200 μg/kg/min for the first 15 minutes to 150 μg/kg/min for the next 15 minutes and 100 μg/kg/min for the remainder of the operation, as tolerated. The concentration of enflurane or the propofol infusion rate was increased or decreased temporarily in increments of 0.5% or 50 μg/kg/min in response to changes in heart rate (HR) or blood pressure (BP) that exceeded 20% of baseline or when there were signs of light anesthesia. Ventilation in both groups was controlled mechanically to maintain an end-tidal carbon dioxide tension ($P_{ET}CO_2$) of 30 to 35 mmHg. Additional vecuronium was administered during the operation if needed, but no additional opioid was given. After the induction of anesthesia, an orogastric Salem Sump tube (Argyle, St. Louis, MO) was placed in each patient to decompress the stomach. This was removed just before the end of the operation after thorough suctioning. Enflurane–N_2O (Group 1) and propofol–N_2O (Group 2) were discontinued simultaneously 2 minutes prior to the end of the operation. The effects of the muscle relaxant were reversed with neostigmine 2.5 mg IV and glycopyrrolate 0.6 mg IV in all patients.

During the induction of anesthesia, the occurrence of pain (stinging, burning, or discomfort) on injection and the time to onset of anesthesia (loss of eyelash reflex and loss of response to verbal command) were recorded. During maintenance of anesthesia, mean arterial pressure (MAP) using a noninvasive automatic device, HR, esophageal temperature, O_2 saturation, and $P_{ET}CO_2$ were monitored and recorded. Emergence from anesthesia was determined by eye opening on command; ability to identify the date of surgery, the hospital, and the patient's date of birth; and the Aldrete score on admission to the postanesthesia care unit. All recovery milestones (emergence, ambulation, voiding, and discharge from the recovery room) were computed from the time of the discontinuation of N_2O and recorded. The same timing instrument was used throughout the study period.

In the recovery room, the blinded observer recorded the occurrence of side effects such as nausea and vomiting, sore throat, and muscle aches, as well as the need for additional opioids such as fentanyl IV or additional antiemetics such as prochlorperazine IV. Each patient repeated the p-deletion and Trieger dot tests at about 60 minutes and again at 90 minutes after the end of anesthesia. The number of lines completed, the number of *p*'s missed, and the number of dots missed were noted.

Preoperatively as well as at the time of discharge, each patient gave her overall assessment using the visual analog scale (VAS) of various perioperative effects, including dizziness, blurred vision, drowsiness, and ability to concentrate. The blinded observer called each patient on the day following surgery to inquire specifically about any side effects (*e.g.*, nausea or vomiting, headache, sore throat, or pain) occurring during transport or while at home. Requirements for analgesics and antiemetics were noted, and intraoperative recall was assessed.

The data obtained from the two groups were compared using analysis of variance (ANOVA), Student's *t*-test, or chi-square analysis as appropriate. A *p*-value of less than 0.05 was considered statistically significant.

Results

There were 30 patients in each group. The two groups (Group 1 *vs.* Group 2) did not differ significantly (ANOVA) in terms of age (32.5 ± 6.4 years *vs.* 30.3 ± 6.0 years), weight (65.4 ± 14.6 kg *vs.* 62.9 ± 6.0 kg), or

Table 1. Emergence and Recovery Times and Nausea and Vomiting in the Postanesthesia Care Unit (PACU)

Variable	Thiamylal-Enflurane (n = 30)	Propofol (n = 30)
Eye opening on command (min)	8.1 ± 5.4	5.2 ± 2.4*
Oriented to day, birth date (min)	12.7 ± 5.1	9.3 ± 3.9*
Time to ambulation (min)	102.7 ± 35.6	83.3 ± 28.6†
Time to voiding (min)	119.5 ± 54.6	101.1 ± 44.4†
Time to discharge (min)	162.1 ± 49.2	138.3 ± 43.0†
Nausea in PACU (n, %)	13 (43.3)	6 (20.0)‡
Vomiting in PACU (n, %)	7 (23.3)	3 (10.0)
Antiemetic Rx in PACU (n, %)	4 (13.3)	1 (3.3)

*$p < 0.01$, ANOVA.

†$p < 0.05$, ANOVA.

‡$p = 0.052$, chi-square analysis.

Note: Data are means ± SD.

height (160.0 ± 7.7 cm *vs.* 160.3 ± 6.0 cm). Average duration of anesthesia was 68.4 ± 16.7 minutes *versus* 69.8 ± 22.0 minutes, and duration of operation was 33.9 ± 12.6 minutes *versus* 37.6 ± 16.3 minutes. These differences were not significant. The time to onset of anesthesia with propofol compared with thiamylal was not significantly different (loss of eyelash reflex, 27.0 ± 13.9 seconds *vs.* 29.9 ± 17.1 seconds; loss of verbal command 24.4 ± 12.2 seconds *vs.* 27.8 ± 15.9 seconds), but significantly more patients receiving propofol complained of pain at the injection site—17 patients (56.7%) *versus* 6 patients (20.0%) (ANOVA, $p < 0.005$). About 90% of the patients in both groups were rendered apneic from the hypnotic drug they received prior to the administration of vecuronium. A transient decrease in BP after induction of anesthesia and a modest increase in HR and MAP were present after tracheal intubation in both groups, but these changes were not significantly different between the groups (ANOVA repeated measures). Thirty percent of the thiamylal-enflurane patients and 26.7% of the propofol patients experienced sinus bradycardia during surgery; one patient in the thiamylal-enflurane group required treatment with atropine.

The times to emergence from anesthesia, voiding, and discharge were all significantly shorter in the propofol group compared with the thiamylal-enflurane group *(Table 1)*. The frequency of nausea in the recovery room was less after propofol anesthesia compared with thiamylal-enflurane anesthesia, with a *p*-value very close to statistical significance ($p = 0.052$) *(Table 1)*. Four patients in the thiamylal-enflurane group needed additional antiemetic therapy in the recovery room, while only one patient in the propofol group needed it.

Patients in both groups were given their first postoperative psychomotor tests about 60 minutes after the discontinuation of N_2O. Patients' scores on these tests were not significantly different from baseline in either group. Likewise, there were no significant differences between the groups at any time tested.

Table 2. Side Effects Up to 24 Hours After Discharge

Variable	Thiamylal-Enflurane (n, %)	Propofol (n, %)
Shoulder pain	13 (43.3)	10 (33.3)
Sore throat	18 (60.0)	17 (56.7)
Nausea	10 (33.3)	9 (30.0)
Vomiting	7 (23.3)	5 (16.7)
Antiemetic Rx needed	0 (0.0)	1 (3.3)

No significant differences between groups, chi-square analysis.

Analysis of the VAS showed no self-perceived differences in dizziness, drowsiness, or ability to concentrate between groups at the time of discharge. We were able to contact all patients 24 hours after the operation. The frequency of side effects was high, although this did not differ significantly between groups *(Table 2)*. No patient had recall of intraoperative events, and there were no serious complications.

Discussion

Several studies that compared propofol to thiamylal or methohexital for induction of anesthesia for short outpatient procedures have found that propofol causes a rapid induction of anesthesia.[2,3,8–11] Several other studies[12–15] compared propofol with isoflurane for maintenance of anesthesia for outpatient surgery. Although isoflurane is a more common inhaled anesthetic for short outpatient operations, many practicing clinical anesthesiologists prefer enflurane because of its lower cost and the lack of demonstrable difference in outcome.[16] We compared propofol with thiamylal-enflurane anesthesia for outpatient operations (laparoscopy). Korttila *et al.*[17,18] also compared propofol anesthesia with enflurane, but for inpatients undergoing laparotomies. Many of the

published studies point to a decrease in postoperative nausea and vomiting with propofol following minor or superficial surgery. However, there are conflicting reports about the frequency of nausea and vomiting following propofol anesthesia, especially after longer operations such as laparoscopies and laparotomies.[13,15,18]

In this study, propofol, like thiamylal, induced anesthesia in one arm-brain circulation time cycle, with similar transient cardiovascular and respiratory depression. A high frequency of pain on injection has been reported by other investigators[19] and may be due in part to the routine placement of the IV cannula in the dorsum of the hand. Use of a larger antecubital vein or the administration of lidocaine 20 mg IV immediately prior to the propofol injection can minimize this problem. The occurrence of pain on injection, though frequent, is rapidly followed by loss of consciousness, and continued pain at the injection site was not reported by any patient postoperatively.

In our study, we did not find any significant difference in hemodynamics (MAP and HR) between propofol and thiamylal-enflurane anesthesia. Gold *et al.*[12] found a significant decrease in systolic blood pressure after propofol during the initial 5 minutes and significant bradycardia throughout the operation. They used triazolam at night and morphine in the morning as premedicants for all their patients. All our patients were healthy (ASA physical status I or II) and received no premedication. Our results in this respect were similar to those of Doze *et al.*[15] and Korttila *et al.*[17] Although we found similar transient hypertension and tachycardia after tracheal intubation in both groups, others[15,17] found less change after propofol compared with thiopental sodium.

Significantly shorter emergence and recovery times (times to ambulation, voiding, and discharge) were the most noteworthy characteristics of the propofol-based anesthesia group. Interestingly, this did not correlate with better scores on the psychomotor tests given 60 minutes after the end of the operation. This is contrary to data from Doze *et al.*[15] who found that patients undergoing nonmajor, superficial surgery who received a propofol *versus* a thiopental-isoflurane anesthetic scored higher on the Trieger dot and p-deletion tests from 30 to 120 minutes postoperatively. In the same study, patients undergoing major intra-abdominal surgery showed no differences in psychomotor test scores in the recovery period. Korttila *et al.*,[13] using three psychomotor tests (perceptual speed, Maddox wing, and tapping board) also found no differences in the time it took patients to return to their baseline scores following outpatient surgery, whether the patient received high-dose propofol (12 mg/kg/hr), low-dose propofol (9 mg/kg/hr), or isoflurane (1%) for their maintenance anesthetic. We found no significant differences in scores at baseline compared with the first administration of the tests postoperatively at 60 minutes in either group. Psychomotor tests given earlier in the postoperative period might have yielded different results. It has been postulated that learning from the preoperative to the postoperative administration of psychomotor tests may have an effect on test scores, thus making the depressant effects of anesthetics difficult to judge.[20]

Despite many advances in our field, nausea and vomiting remain the most common side effects following anesthesia for outpatient surgery.[21] When present, they invariably cause a delay in discharge from the hospital.[22] Several studies in outpatients (with surgery not limited to laparoscopy) report significantly less nausea and vomiting following a propofol-based anesthetic *versus* an isoflurane-based technique.[15,18] Data from Korttila *et al.*[18] suggest that this may be a dose-related phenomenon: patients receiving low-dose propofol (9 mg/kg/hr) had significantly less nausea and vomiting than patients receiving either high-dose propofol (12 mg/kg/hr) or thiopental sodium–isoflurane (1%). Doze *et al.*[15] reported significantly less nausea and vomiting following a propofol-based *versus* an isoflurane-based anesthetic in outpatients undergoing superficial, nonmajor surgery but found no such decrease in inpatients undergoing major (*e.g.*, intra-abdominal) surgery. Before the introduction of propofol to clinical practice, many studies[4,5] reported that the frequency of nausea and vomiting in female patients undergoing laparoscopy was very high (about 50%). That is why we considered it unfair to the patient not to administer a prophylactic antiemetic in this high-risk group. Patients in both groups received droperidol 0.6 mg before induction of anesthesia. In spite of this, our study revealed a strong trend toward less nausea and vomiting following propofol anesthesia. The frequency of other side effects, such as sore throat, shoulder pain, and postdischarge nausea and vomiting, was disturbingly high in both groups. Again, this may be due in part to the nature of the surgery; similar findings have been reported by other investigators.[23]

We conclude that propofol is a useful anesthetic drug for outpatient surgery. It is comparable to thiopental sodium–enflurane in terms of its smooth onset and hemodynamic stability. The shorter recovery time following the use of propofol give it a distinct advantage in the outpatient population.

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