Induction with sevoflurane-remifentanil is comparable to propofol-fentanyl-rocuronium in PONV after laparoscopic surgery

[L'induction avec sévoflurane-rémifentanil ou propofol-fentanyl-rocuronium est similaire quant aux NVPO en chirurgie laparoscopique]

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Purpose: To compare sevoflurane-remifentanil induction and propofol-fentanyl-rocuronium induction with regards to the frequency of moderate to severe postoperative nausea and vomiting (PONV) in the first 24 hr after laparoscopic day surgery.

Methods: After informed consent, 156 ASA physical status class I to III patients undergoing laparoscopic cholecystectomy or tubal ligation were randomized to either induction with sevoflurane 8%, N_2O 67% and *iv* remifentanil 1 to 1.5 $\mu g \cdot kg^{-1}$ or induction with *iv* fentanyl 2 to 3 $\mu g \cdot kg^{-1}$, propofol 2 $mg \cdot kg^{-1}$, and rocuronium 0.3 to 0.5 $mg \cdot kg^{-1}$. All patients received *iv* ketorolac 0.5 $mg \cdot kg^{-1}$ at induction and sevoflurane-N_2O maintenance anesthesia with rocuronium as needed. PONV was treated with *iv* ondansetron, droperidol, or dimenhydrinate; postoperative pain was treated with opioid analgesics. Patients were followed for 24 hr with regards to PONV and pain. Intubating conditions, induction and emergence times, time to achieve fast-track discharge criteria, and drug costs were measured.

Results: No differences were seen between the two groups in their frequencies of 24-hr moderate to severe PONV and postoperative pain, or in their intubating conditions, induction and emergence times, and time to achieve fast-track discharge criteria. Patients undergoing sevoflurane-remifentanil induction received more morphine (11 mg *vs* 8 mg; *P* < 0.001) in the postanesthetic care unit. Sevoflurane-remifentanil induction resulted in similar anesthetic and total drug costs for both procedures.

Conclusion: We did not demonstrate any difference in PONV, pain, or anesthetic/recovery times or costs between the sevoflurane and propofol groups. Sevoflurane-remifentanil induction is a feasible technique for anesthetic induction.

Objectif : Comparer l'induction avec sévoflurane-rémifentanil ou propofol-fentanyl-rocuronium quant à la fréquence de nausées et vomissements postopératoires (NVPO) de modérés à sévères pendant les 24 premières heures après une opération en chirurgie d'un jour sous laparoscopie.

Méthode : Après avoir accordé leur consentement, 156 patients d'état physique ASA I à III devant subir une cholécystectomie laparoscopique ou une ligature des trompes ont été randomisés pour une induction avec du sévoflurane à 8 %, N_2O à 67 % et 1 à 1,5 $\mu g \cdot kg^{-1}$ de rémifentanil iv ou une induction iv avec 2 à 3 $\mu g \cdot kg^{-1}$ de fentanyl, 2 $mg \cdot kg^{-1}$ de propofol et 0,3 à 0,5 $mg \cdot kg^{-1}$ de rocuronium. Tous les patients ont reçu 0,5 $mg \cdot kg^{-1}$ de kétorolac iv à l'induction et un mélange de sévoflurane-N_2O pour le maintien de l'anesthésie, avec rocuronium au besoin. Un traitement iv avec ondansétron, dropéridol ou dimenhydrinate a été donné pour les NVPO et la douleur postopératoire a été soulagée avec des analgésiques opioïdes. Les patients ont été suivis pendant 24 h pour les NVPO et la douleur. Ont été notés : les conditions d'intubation, les temps nécessaires à l'induction et au réveil, le temps d'atteindre les critères de congé de la chirurgie ambulatoire et le coût des médicaments.

Résultats : Aucune différence intergroupe n'a été enregistrée concernant la fréquence de NVPO de modérés à sévères et la douleur postopératoire pendant 24 h, ou les conditions d'intubation, les temps d'induction et de réveil, de même que le temps nécessaire à l'atteinte des critères de congé. Les patients soumis à une induction avec un mélange de sévoflurane-rémifentanil ont demandé plus de morphine (11 mg *vs* 8 mg ; *P* < 0,001) en salle de réveil. L'induction avec sévoflurane-rémifentanil a conduit à un usage d'anesthésiques et à un

coût total de médicaments similaires pour les deux types d'interventions chirurgicales.

Conclusion : *Nous n'avons trouvé aucune différence de NVPO, de douleur ou de temps liés à l'analgésie et à la récupération postopératoires entre les groupes sous sévoflurane ou propofol. Un mélange de sévoflurane-rémifentanil peut servir à l'induction de l'anesthésie.*

POSTOPERATIVE nausea and vomiting (PONV) remains an important and frequent complication following surgery and anesthesia. In the ambulatory setting, PONV is one of the most significant factors predicting prolonged postoperative stay and unanticipated admissions.[1,2] Additionally, PONV is a strong negative influence upon a patient's postoperative function[3] and satisfaction.[4]

The frequency of PONV in the ambulatory setting varies significantly, depending on the type of surgery, patient characteristics, and type of anesthesia. For patients undergoing minor gynecological surgery, the risk of nausea and vomiting is 75% and 61% respectively.[5] In laparoscopic cholecystectomy, the frequency (without prophylactic antiemetics) was reported to be 72% in one randomized controlled trial.[6] In the presence of prophylactic antiemetics, the frequency decreased, but remained significant, within a range of 30% to 60% depending on the type of study.[7–9] Female gender, history of motion sickness or PONV, and a negative smoking history are also risk factors for PONV.[1,3] In general, these characteristics are not amenable to modification in the preoperative setting.

A number of anesthetic factors may influence the risk of PONV. Omission of N_2O significantly reduced PONV in several meta-analyses,[10–13] but the risk of intraoperative awareness was also increased.[12] In most meta-analyses, propofol was associated with a lower frequency of PONV when used for total *iv* anesthesia in the absence of N_2O.[12–15] In one meta-analysis, the rate of PONV was lower with the use of any propofol when compared with sevoflurane.[16] The omission of anticholinesterases (for reversal of muscle relaxation) also reduced PONV but also resulted in an increased risk of clinically relevant residual muscle weakness.[17] Postoperative use of opioid analgesics was also associated with an increased frequency of PONV.

Ideally, for general anesthesia in the ambulatory laparoscopic population, one would choose an agent with rapid onset and elimination that would provide adequate amnesia and muscle relaxation for the surgical procedure. For analgesia in mild to moderately painful procedures, if opioids are needed, the agent should also have rapid onset and elimination. Postoperative analgesia would then be achieved via non-opioid analgesics, such as nonsteroidal anti-inflammatory drugs, with longer lasting opioids used for breakthrough pain.

The desired properties of a general anesthetic, as highlighted above, may be achieved with sevoflurane and remifentanil. The use of sevoflurane as the sole anesthetic agent for induction and maintenance provides adequate intubating conditions without the use of muscle relaxants. Numerous reports have also demonstrated similar intubating conditions, in the absence of muscle relaxants, using remifentanil and propofol as the co-induction agents.[18–24] Recently, induction with remifentanil and sevoflurane has enabled rapid endotracheal intubation without the use of muscle relaxants.[25]

What remained to be seen was whether sevoflurane-remifentanil induction, a novel technique, would decrease the frequency of PONV compared to standard practice. The primary objective of this study was to determine the frequency of PONV with the use of sevoflurane-remifentanil induction compared to propofol-fentanyl-rocuronium induction in ambulatory patients undergoing laparoscopic surgery.

Methods

This study was conducted in two tertiary care, academic hospitals (Hamilton Health Sciences - McMaster site and St. Joseph's Hospital) in Hamilton, Ontario. After Institutional Research Ethics Board approval and informed consent, we enrolled patients undergoing laparoscopic cholecystectomy or laparoscopic tubal ligation[A] who met the following criteria: weight ≤ 100 kg, body mass index ≤ 35 kg·m^{-2}, age > 16 yr, ASA physical status class $\leq$ III, and elective procedure booked for same-day discharge. Patients were excluded if they had participated in another study with an experimental drug within the month prior to enrollment, were pregnant or breastfeeding, had received medications with anti-emetic properties within 48 hr of surgery, or had contraindications to the anesthetic techniques or the medications used in this study.

Using a random numbers table, stratified by centre and procedure, patients were allocated, upon entry into the operating room, to sevoflurane-remifentanil induction (sevoflurane group) or propofol-fentanyl-rocuronium induction (propofol group). The anesthesiologists and operating room nurses were not blinded

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A   Laparoscopic tubal ligations were performed at the Hamilton Health Sciences only.

but patients were not informed of the induction technique that they received. A restricted group of 12 anesthesiologists, competent in the sevoflurane-remifentanil induction technique, performed all the anesthetics to ensure consistency. We did not exclude any general surgeon or gynecologist from participating nor did we control the laparoscopic techniques used. The surgical team was blinded to the induction technique. The postoperative data collectors and the data analysts were blinded to the intervention.

In the sevoflurane group, a vital capacity induction technique (sevoflurane 8%, N_2O 2 L·min^{-1}, O_2 1 L·min^{-1}) was used to obtain loss of consciousness, followed by a 30-sec iv injection of remifentanil 1 to 1.5 µg·kg^{-1}. One minute after remifentanil administration, tracheal intubation was attempted. Sevoflurane and additional boluses of remifentanil 0.5 µg·kg^{-1} iv were used to maintain anesthesia until intubation was successful. Once the trachea was intubated, anesthesia was maintained with N_2O 1.3 L·min^{-1}, O_2 0.7 L·min^{-1}, and sevoflurane as per the anesthesiologist. Rocuronium 0.15 mg·kg^{-1} iv was used if muscle relaxation was inadequate with sevoflurane alone. Remifentanil was not administered after endotracheal intubation.

In the propofol group, patients received fentanyl 2 to 3 µg·kg^{-1} iv one minute prior to induction, followed by propofol 2 mg·kg^{-1} iv and rocuronium 0.3 to 0.5 mg·kg^{-1} iv for induction. One minute later, tracheal intubation was attempted. Additional boluses of propofol 1 mg·kg^{-1} iv or fentanyl 1 to 2 µg·kg^{-1} iv were given as needed until the trachea could be intubated. Anesthesia was maintained with N_2O 1.3 L·min^{-1}, O_2 0.7 L·min^{-1}, and sevoflurane as per the anesthesiologist. Supplemental boluses of fentanyl 1 to 2 µg·kg^{-1} iv were given as needed for analgesia at the discretion of the patient's anesthesiologist based on clinical signs and symptoms (e.g., tachycardia, hypertension, pupillary dilatation). Supplemental boluses of rocuronium 0.15 mg·kg^{-1} iv were given as needed for muscle relaxation based on neuromuscular train-of-four monitoring.

No patient received any prophylactic anti-emetic, analgesic, or anxiolytic. In both groups, ketorolac 0.5 mg·kg^{-1} (maximum 30 mg) iv was given for pre-emptive analgesia at induction. In patients who received rocuronium, reversal of neuromuscular blockade was achieved with neostigmine 30 to 50 µg·kg^{-1} iv and glycopyrrolate 5 to 8 µg·kg^{-1} iv. Anesthesia was terminated at the end of the surgery.

In the postanesthetic care unit, patients received morphine 2 to 4 mg iv every five minutes, to a maximum total dose of 0.3 mg·kg^{-1}, as needed for analgesia. Meperidine 25 to 50 mg iv every 15 min, to a maximum total dose of 1 mg·kg^{-1}, was used as the second-line analgesic. PONV was treated with droperidol 25 µg·kg^{-1} iv or ondansetron 4 mg iv. During this study, Health Canada released a bulletin concerning potential cardiac complications with the use of droperidol.[26] At that point, the use of droperidol was discontinued and ondansetron was used as the first-line rescue anti-emetic. Dimenhydrinate 0.25 to 0.5 mg·kg^{-1} iv was used as the second-line rescue anti-emetic. For postdischarge analgesia, prescriptions for Tylenol #2 (acetaminophen 325 mg/codeine 20 mg) tablets and Tylenol #3 (acetaminophen 325 mg/codeine 30 mg) tablets were given to patients after laparoscopic cholecystectomy and laparoscopic tubal ligation respectively.

Measurements and statistical analysis

The primary outcome of this study was the frequency of moderate to severe PONV over the first 24 hr after surgery. Severity of PONV was measured using a 10-cm visual analogue scale (VAS) with scores greater than 3 considered to be moderate to severe. Secondary outcomes included moderate to severe pain over the first 24 hr after surgery (measured using a 10-cm VAS similar to PONV measurements), ease of intubation (measured using a six-item, 12-point score, Table I), anesthetic induction and emergence times, time required to achieve fast-track criteria,[27] amount of postoperative anti-emetics and analgesics used, and total drug costs. Intraoperative data were recorded by

TABLE I Factors evaluated to determine ease of intubation. Intubating score is based on the consensus conference on good clinical research practice in pharmacodynamic studies of neuromuscular blocking agents[32]

| Factor	0 point	1 point	2 points
Manual ventilation prior to intubation	Easily ventilated	Some difficulty	Great difficulty
Jaw relaxation	Relaxed	Opens with some difficulty	Opens with great difficulty
Ease of laryngoscopy	Easy	Some difficulty	Great difficulty
Vocal cords	Open without movement	Some movement	Completely closed
Coughing during intubation	None	≤ 2 coughs	> 2 coughs
Limb movement	None	Flicker of movement	Significant movement
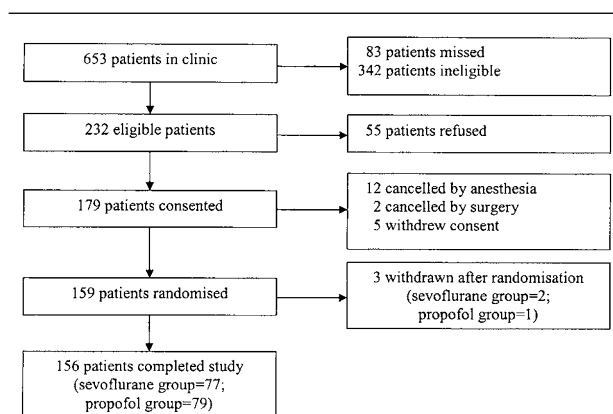
FIGURE 1 Summary of trial profile.

the patient's anesthesiologist; postoperative data were measured by a blinded research assistant. To determine drug costs, we assumed that leftover medications from a case would be thrown out at the end of the case with the exception of remifentanil, in which the required dose would be drawn from a premixed bag (1 mg in 100 mL of normal saline), which was the clinical practice at the time of the study. Similarly, we assumed that leftover anti-emetics or analgesics would be discarded in the postoperative period in hospital.

Sample size calculation was based on an expected frequency of 60% for moderate to severe PONV in the propofol group, 27% absolute risk reduction (45% relative risk reduction), a 5% two-sided type I error rate, and 90% power. After accounting for stratification by centre and surgical procedure and an anticipated 5% withdrawal rate, 78 patients per group were required. A power analysis indicated that this sample size would detect an absolute difference of 23.5% with 80% power and an absolute difference of 21% with 70% power.

The Mantel-Haenszel Chi-square statistic was used to compare the two groups for the primary outcome with the results expressed as proportions and odds ratios (OR) with 95% confidence intervals (CI). A multivariate analysis was conducted to determine the effect of PONV risk factors,[28] surgical procedure, and study centre on PONV. The primary analysis was adjusted for those factors that were found to be statistically significant in the multivariate analysis. A *P* value < 0.05 was considered to be statistically significant for the primary outcome.

For secondary outcomes, dichotomous data were expressed as proportions and OR with 95% CI and were compared using the Chi-square statistic or

Fisher's exact test where appropriate. Normally distributed, continuous data were expressed as means and standard deviations and were compared using the two-sided t test. Non-normally distributed, continuous data were expressed as medians and were compared using the Wilcoxon rank sum test. Given the multiple comparisons, a Bonferroni correction was made; a *P* value of < 0.005 was considered statistically significant.

The investigators, including the anesthesiologists, pharmacists, and research nurses were presented with the blinded results, as "Group A" and "Group B," for interpretation. The group allocations were unmasked only after the interpretation was completed. Because between-group comparisons of the amounts and costs of individual intraoperative drugs would unmask the allocation and unblind the data analyst, we did not make any comparisons of specific drug amounts or costs during the initial blinded analysis. *Post hoc* unblinded analyses of the costs for specific drugs were made.

Results

Figure 1 summarizes the trial profile. One hundred and fifty-nine patients were randomized during the study; however, one patient had clinical signs strongly predictive of a difficult intubation, which was missed during the preoperative assessment clinic visit but detected prior to induction, one patient had severe nausea prior to induction, and one patient did not undergo the scheduled procedure. In total, 156 patients completed the study. There were no statistically significant differences in the physical characteristics or the distribution of PONV risk factors between the two groups (Table II).

The number of PONV risk factors was a significant predictor of PONV but the number of days after menses, in menstruating women, was not. The overall frequency of moderate to severe PONV over 24 hr was high (44.8%); however, the frequency in the sevoflurane group (41/77; 53.2%) was not significantly different from the frequency in the propofol group (29/79; 36.7%) with an OR, adjusted for the number of PONV risk factors, of 1.79 (95% CI 0.92 to 3.38; *P* = 0.12). There were no significant differences in the frequency of moderate to severe PONV over 24 hr between the two anesthetic techniques in the laparoscopic cholecystectomy and laparoscopic tubal ligation subgroups.

The frequency of moderate to severe postoperative pain over 24 hr was not significantly different between the sevoflurane (70/77; 90.9%) and the propofol (66/79; 83.5%) groups (OR 1.97; 95% CI 0.74 to 5.24; *P* = 0.26). The number of PONV risk factors,

TABLE II Physical characteristics and distribution of postoperative nausea and vomiting risk factors between groups

Characteristic*	Sevoflurane group (n = 79)	Propofol group (n = 80)
Age (yr)	37.5 ± 11.1	38.7 ± 10.9
Height (cm)	161.7 ± 19.2	166.1 ± 8.0
Weight (kg)	68.6 ± 14.3	72.3 ± 13.2
PONV risk factors		
Female (%)	72 (91.1)	68 (85.0)
Motion sickness (%)	21 (26.6)	10 (12.5)
PONV (%)	27 (34.2)	23 (28.8)
Non-smoking status (%)	25 (31.6)	31 (38.8)
Number of risk factors (0/1/2/3)†	0/17/35/26	5/21/39/15
Time in menstrual cycle		
0 to 8 days after menses (%)	20 (27.8)	17 (25.0)
9 to 16 days after menses (%)	11 (15.3)	14 (20.6)
> 16 days after menses (%)	26 (36.1)	20 (29.4)
On hormone replacement (%)	2 (2.8)	5 (7.4)
Post-menopausal (%)	10 (13.9)	8 (11.8)
Unclear (%)	3 (4.2)	4 (5.9)
Laparoscopic cholecystectomy	32 (41.6)	35 (44.3)
Laparoscopic tubal ligation	45 (58.4)	44 (55.7)

*Continuous variables are expressed as means ± standard deviations; discrete variables are expressed as absolute number and percentages. †Motion sickness or postoperative nausea and vomiting (PONV) were counted as one risk factor.
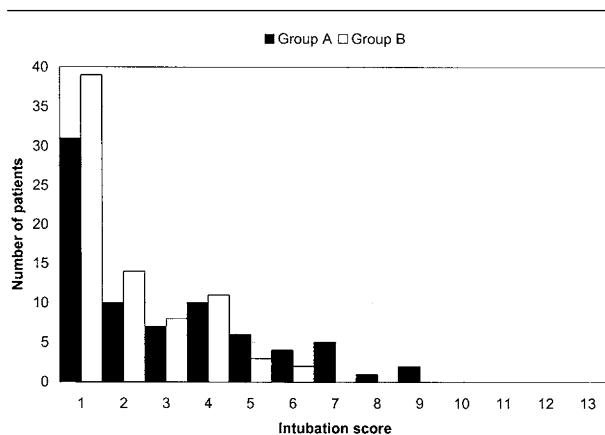

FIGURE 2 Bar chart of intubation scores by type of anesthetic induction. Group A = sevoflurane group; Group B = propofol group.
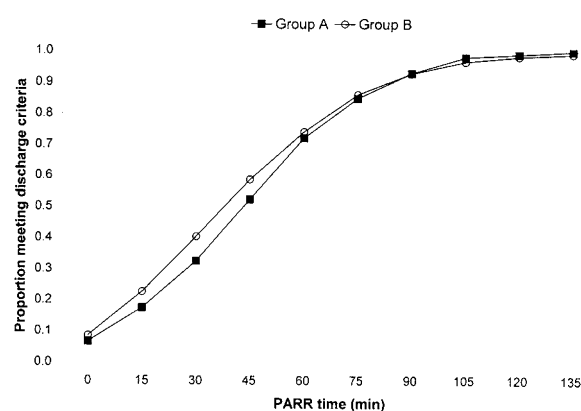

FIGURE 3 Kaplan-Meier plot of fast-track discharge eligibility over time by type of anesthetic induction. Group A = sevoflurane group; Group B = propofol group.

the number of days after menses, and the surgical procedure did not affect the result. No adverse events were seen resulting from anesthesia.

Intubating conditions were not significantly different between the two anesthetic techniques (Figure 2). Induction times (sevoflurane 3.4 ± 2.2 min *vs* propofol 3.2 ± 3.0 min; *P* = 0.49) and emergence times (sevoflurane 4.2 ± 2.4 min *vs* propofol 4.5 ± 2.0 min; *P* = 0.39) were not significantly different between the two groups. Time to reach fast-track discharge criteria was not significantly different (Figure 3; *P* = 0.08) with a median time of 45 min for both groups; however, discharge from the postanesthetic care unit was often delayed due to non-medical factors. The type of surgery did not affect these findings.

The amounts of anti-emetics, meperidine, and acetaminophen-codeine used per patient in the postanesthetic care unit, in hospital, and during 24 hr were not significantly different between the two groups. The amount of morphine used was higher in the sevoflurane group (11 mg) than in the propofol group (8 mg; *P* < 0.001) in the postanesthetic care unit. Sevoflurane-remifentanil induction followed by sevoflurane maintenance anesthesia was comparable to propofol-fentanyl-rocuronium induction followed by sevoflurane maintenance anesthesia ($34.21 *vs*

$38.29; *P* = 0.089) and did not significantly increase the costs of postoperative anti-emetic and analgesic use (sevoflurane group $25.72 *vs* propofol group $17.27; *P* = 0.028). The difference in intraoperative anesthetic drug costs was not statistically significant for either types of surgery (Table III). Overall, the total drug cost in the sevoflurane group was not significantly different from the propofol group ($56.81 *vs* $46.78; *P* = 0.045).

TABLE III Drug costs by type of anesthetic and surgery

	Sevoflurane group	Propofol group	Difference (95% CI)*
Intraoperative drug costs			
All patients	$34.21	$38.29	$4.08 (-$0.63 to $8.80)
Sevoflurane	$23.84	$10.39	-$13.45 (-$17.12 to -$9.78)†
Intraoperative opioids‡	$1.19	$0.82	-$0.38 (-$0.50 to -$0.24)†
Rocuronium	$4.41	$13.07	$8.66 ($7.08 to $10.23)†
Neostigmine and glycopyrrolate	$1.70	$6.24	$4.54 ($3.87 to $5.21)†
Laparoscopic cholecystectomy	$47.65	$44.71	-$2.94 (-$10.35 to $4.48)
Laparoscopic tubal ligation	$24.65	$33.18	$8.53 ($4.83 to $12.24)
Postoperative drug costs			
All patients	$25.72	$17.27	-$8.45 (-$15.96 to -$0.94)
Antiemetics	$3.50	$2.90	-$0.59 (-$1.83 to $0.64)
Analgesics	$21.90	$14.48	-$7.41 (-$14.49 to -$0.34)
Laparoscopic cholecystectomy	$37.27	$21.06	-$16.22 (-$31.09 to -$1.34)
Laparoscopic tubal ligation	$17.55	$13.79	-$3.78 (-$9.87 to $2.35)
Total drug costs			
All patients	$56.81	$46.78	-$10.03 (-$19.82 to -$0.23)
Laparoscopic cholecystectomy	$81.06	$58.13	-$22.94 (-$39.25 to -$6.64)
Laparoscopic tubal ligation	$39.22	$36.35	-$2.87 (-$10.07 to $4.34)

*Note that 95% confidence intervals (CI) are reported but $P < 0.001$ is considered statistically significant due to the multiple comparisons. †$P < 0.001$. ‡Remifentanil in the sevoflurane group; fentanyl in the propofol group.

Discussion

We did not find a statistically significant difference in 24-hr moderate to severe PONV between sevoflurane-remifentanil induction and propofol induction. Our sample size had 84% power to detect an absolute difference of 16.5%, seen in this study, and 90% power to detect an absolute difference of 25.6% with a type I error rate of 5%. Given our findings, we would have required 198 patients to achieve statistical significance with 90% power.

In terms of secondary clinical outcomes, there were no differences in 24-hr moderate to severe postoperative pain, intubating conditions, induction and emergence times, and time to achieve fast-track discharge criteria. These findings were consistent with the subjective impressions of the anesthesiologists and the blinded postoperative caregivers. Previous concerns with potential delays in endotracheal intubations using sevoflurane induction did not seem to be a problem in this study with the use of remifentanil. A post-trial survey of the individuals involved with the clinical care of the patients showed that 80% (28/35) felt there was no subjective difference between the two groups in terms of PONV or postoperative pain.

In terms of secondary pharmacoeconomic outcomes, patients in the sevoflurane group received an extra 3 mg of *iv* morphine postoperatively. Although the difference was statistically significant, we are doubtful of its clinical or economical ($0.05) significance.

Compared to the propofol group, we did not find any statistically significant difference in intraoperative anesthetic drug costs, postoperative drug costs, or total 24-hr drug costs for all patients in the sevoflurane group. A trend towards increased postoperative drug costs and total 24-hr drug costs in patients undergoing laparoscopic cholecystectomy was seen in the sevoflurane group. In contrast, lower intraoperative drug costs[29,30] and perioperative costs[30] with sevoflurane induction were reported in previous clinical trials comparing sevoflurane and propofol induction. Different surgical procedures may explain the differences between our results and those of previous trials.

In this study, we did not detect a difference in costs, clinical outcome, anesthetic time, and recovery time between the two induction techniques. We suggest that more research in the pharmaco-economics *vs* clinical outcome in various outpatient surgical populations is necessary. It is worth noting that with the use of prophylactic anti-emetics, such as ondansetron, the sample size required would be significantly larger in order to study the clinical and economical trends observed in this study. For example, if we assume an event rate of 20% with the use of prophylactic ondansetron and propofol induction (based on 36.7% risk of PONV in this study and an absolute risk reduction of 16.7% with prophylactic ondansetron),[31] we would need 308 subjects to detect an absolute difference of 16.5% (based on 53.2% risk of PONV in this

study and an absolute risk reduction of 16.7% with prophylactic ondansetron)[31] between sevoflurane and propofol induction with 5% type I error rate and 90% power. Most studies are underpowered to detect such a difference.

In summary, compared to propofol-fentanyl-rocuronium induction, sevoflurane-remifentanil induction was a clinically feasible technique for laparoscopic cholecystectomy and laparoscopic tubal ligation without causing a statistically significant difference in 24-hr moderate to severe PONV. We did not find any clinically significant differences in secondary outcomes, induction time, emergence time, recovery time, or costs.

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