Target Controlled Infusion versus Sevoflurane/Desflurane Anesthesia for Laparoscopic Cholecystectomy: Comparison Postoperative Nausea/Vomiting and Extubation Time

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Background: *Target-controlled infusion (TCI) systems have been developed from manually controlled infusion systems and have rapidly increased in popularity, especially in laparoscopic surgery. Propofol is claimed to decrease nausea and vomiting.*

Objective: *To compare anesthetic techniques, propofol-TCI, desflurane, and sevoflurane, for better results in terms of postoperative nausea and vomiting (PONV) and extubation times.*

Material and Method: *The present study was prospective with informed consent from 75 patients, ASA 1-3 scheduled for laparoscopic cholecystectomy, and classified by anesthetic technique into three groups. The patients were induced by propofol target plasma concentration 6 µg/ml in Group P, or 1-2 mg/kg in Group S and Group D, fentanyl 2 µg/kg and vecuronium 0.1 mg/kg followed by propofol 2 to 5 µg/ml in group P, sevoflurane 0.5 to 3% in Group S, and desflurane 2 to 6% in Group D.*

Results: *The incidence of postoperative nausea and vomiting was least in Group P, both at the PACU ($p<0.001$) and ward ($p = 0.01$). Extubation time excluding outlier were Group P 11.17±1.19 minutes, Group D 13.96±1.17 minutes, Group S 11.75±1.34 minutes ($p = 0.25$). There were no statistical differences in the amount of fentanyl ($p = 0.38$) and fluid replacements ($p = 0.05$).*

Conclusion: *Laparoscopic cholecystectomy under propofol with TCI is one option of anesthetic technique with a significantly lower incidence of PONV compared with both sevoflurane and desflurane otherwise there is no statistical difference in the extubation time. Propofol-TCI technique is suggested for laparoscopic and ambulatory surgery.*

Keywords: *Laparoscopic cholecystectomy, Propofol, Target-controlled infusion, Postoperative nausea/vomiting, Extubation time*

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Total Intravenous Anesthesia (TIVA) technique consists of two techniques, Target-Controlled Infusion (TCI) systems and Manually Controlled Infusion (MCI) system. TCI systems have been developed from MCI system and have rapidly increased in popularity, especially in laparoscopic surgery. We usually use propofol combined with opioids in the TIVA technique with recommended dose[1,2]. The amount of propofol in TCI system is used more than MCI system but the patients have no the awareness[3]. TCI system monitors blood concentrations so the patients have optimized anesthetic depth.

Propofol is claimed to effect on 5-HT3 receptor antagonist to decrease nausea and vomiting[4]. Volatile agents produce pollution, precipitate malignant hyperthermia, and the incidence of postoperative nausea and vomiting (PONV)[5]. Therefore, propofol-TCI has benefits in the patients with a history of PONV and history or family history of malignant hyperthermia who come for general anesthesia. There are some studies compared the benefits of TIVA/TCI technique rather than volatile technique[6-17] but not the model we studied. The aim of the present study was to compare anesthetic techniques for better results in terms of PONV and extubation times.

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Material and Method

After approval by the Songklanagarind Hospital's Ethics Committee, the 75 patients with ASA classification 1-3, age 18 to 70 years old, scheduled for elective laparoscopic cholecystectomy gave informed consent to participate in the present study. The patient anonymity was preserved. We registered

the protocol in ClinicalTrials.gov before the first patient was recruited. The patients who had a history of dizziness, took an antiemetic drug 24 hours before surgery, had chronic obstructive pulmonary disease (COPD), required rapid sequence induction or had an allergy to propofol, fentanyl, or vecuronium were excluded. All patients were premedicated with diazepam 5 to 10 mg orally, one hour before induction. Pre-oxygenation with 100% 5 L/minute and preload crystalloid 7 ml/kg were given before induction as well.

Seventy-five patients were randomized into three groups by computer with 25 patients in each. Group P (TCI) was administered propofol by TCI system (Injectomat TIVA, Agilia, Fresenius Kabi) induced by plasma concentration 6 µg/ml, fentanyl 2 µg/kg, and vecuronium 0.1 mg/kg before endotracheal intubation. Maintenance of anesthesia, adjusted by propofol's plasma concentration 2 to 5 µg/ml. Propofol infusion was discontinued during wound closure. Group D (Desflurane) and Group S (Sevoflurane) were induced by propofol 1 to 2 mg/kg, fentanyl 2 µg/kg and vecuronium 0.1 mg/kg, N_2O 66%, and O_2 33% total flow 1 to 2 L/minute were administered for the maintenance of anesthesia in both groups, desflurane 2 to 6% and sevoflurane 0.5 to 3%. Volatile agent delivery was stopped during wound suture. Electrocardiogram, arterial blood pressure, mean arterial blood pressure, and heart rate were recorded before and after induction, before and after incision, and before and after extubation. If the patients had a systolic blood pressure less than 90 mmHg or less than 30% of the normal range, ephedrine 6 mg or levophed 10 mg was administered intravenously. If the heart rate was lower than 45 beat/minute and the patient had hypotension, atropine 0.6 mg was administered. Drug doses including propofol, fentanyl, vecuronium, fluid replacement, ephedrine, and atropine were recorded. Extubation times, the time from TCI or when volatile agents were stopped until extubation were recorded.

After surgery, all patients were transferred to the postanesthesia care unit (PACU). Aldrete score were recorded. The patients were discharged if they had an Aldrete score ≥8. Nausea and vomiting were graded by 0 to 3, 0 is nil episodes of nausea and vomiting, 1 is mild nausea only, 2 is nausea or vomiting requiring only initial treatment, 3 is nausea or vomiting requiring repeated treatment. Ondansetron or metroclopramide was administered for nausea and vomiting at PACU and the ward and total amounts of drug doses were recorded.

Sample size calculation

The sample sizes were based on previous studies of Stosic et al[13], propofol-TCI with laparoscopic cholecystectomy with type I error of 0.05 and a power of 80%. The sample sizes were calculated to be 22 patients each group were for PONV and seven patients each group for extubation time. We used 22 patients/group combined with a 10% drop out for detecting the difference.

Statistical analysis

The data was analyzed by Program R version 2.11.0. Each variable was analyzed by ANOVA test. Chi-square and Fisher's exact test were used to analyze for category variables. Wilcoxon Rank sum test and student t-test were used for continuous variables. Age and fluid were analyzed by multivariate analysis.

Results

There were no differences of patient characteristics among the groups regarding sex (p = 0.55) and ASA classification (p = 0.63), BMI (p = 0.15), and surgery time (p = 0.20). The patients in Group P were older than Group D and Group S by chance (p = 0.02) (Table 1). There were no statistical differences in the amount of fentanyl (p = 0.38), vecuronium (0.05), and fluid replacements (0.05)

Table 1. Patient characteristics

	Group P	Group D	Group S	*p*-value
Sex (male/female)	7/18	11/24	9/16	0.55
ASA classification (I/II/III)	6/15/14	2/23/0	3/21/1	0.06
BMI (kg/m^2)	24.88±3.10	23.20±4.52	25.20±4.40	0.15
Age (years)	56.08±8.93	47.64±15.73	43.04±10.38	0.01
Time of surgery (minutes)	104.90±43.64	91.12±36.85	120.60±40.45	0.20

ASA = American Society of Anesthesiologist; BMI = body mass index
Data as number or mean ± SD

among three groups (Table 2). Fluid replacement in each group was showed in Table 1.

The incidence of postoperative nausea and vomiting was least in Group P both at PACU and ward (p<0.001 and 0.01, respectively). The patients in Group D required antiemetic drugs less than the patients in Group S at PACU. The patients in Group S required antiemetic drugs less than the patients in Group D at ward. Both showed no significant statistical differences (Table 3).

The times (mean ± sem) from the end of the administration of anesthetics to tracheal extubation was longest in Group P 17.04±11.97 minutes, followed by Group D 13.52±13.07 minutes and Group S 13.04±9.6 minutes respectively (p = 0.21). Extubation time excluding outlier were Group P 11.17±1.19 minutes, Group D 13.96±1.17 minutes, Group S 11.75±1.34 minutes (p = 0.25) showed in Fig. 1.

Vital signs including systolic blood pressure, diastolic blood pressure, mean arterial pressure and heart rate were recorded before/after the intubation,

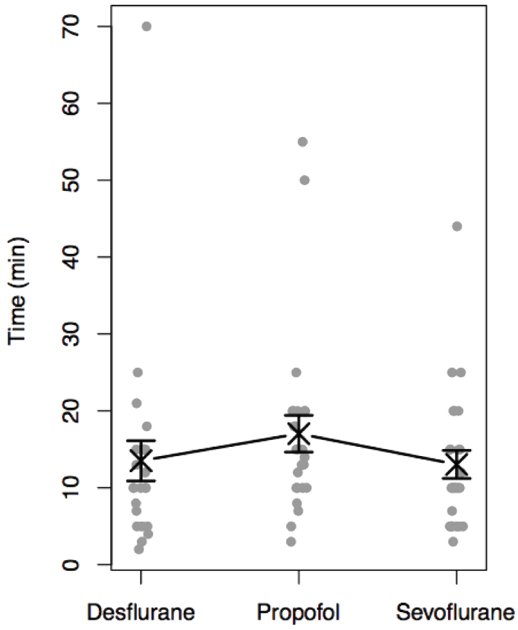

Fig. 1 Extubation time classified by anesthetic agent.

Table 2. Drug doses in each group

	Group P	Group D	Group S	p-value
Propofol (mg)	933.84±295.81	127.20±25.74	161.88±104.76	N/A
Fentanyl (mcg)	130.80±47.71	116.80±32.04	120.21±29.98	0.38
Vecuronium (mg)	7.52±1.53	6.40±1.71	7.46±1.98	0.05
Fluid replacement (ml)	1,280.00±705.80	932.00±445.30	1,054.00±261.80	0.05

N/A = not available
Data as mean ± SD

Table 3. Incidence of postoperative nausea and vomiting

		Desflurane	Propofol	Sevoflurane	p-value
PACU					
Grade	0	23 (92.0)	23 (92.0)	11 (44.0)	<0.001
	1	1 (4.0)	1 (4.0)	5 (20.0)	
	2	1 (4.0)	1 (4.0)	9 (36.0)	
Ondansetron (mg)	0	23 (92.0)	23 (92.0)	15 (60.0)	0.01
	4	2 (8.0)	1 (4.0)	7 (28.0)	
	8	0 (0.0)	1 (4.0)	3 (12.0)	
Ward					
Grade	0	17 (68.0)	25 (100.0)	23 (92.0)	0.01
	1	6 (24.0)	0 (0.0)	1 (4.0)	
	2	2 (8.0)	0 (0.0)	1 (4.0)	
Ondansetron (mg)	0	22 (88.0)	25 (100.0)	24 (96.0)	0.32
	4	1 (4.0)	0 (0.0)	0 (0.0)	
	8	2 (8.0)	0 (0.0)	1 (4.0)	

PACU = post Anesthetic Care Unit
Data as number (%)

before/after the incision and before/after the extubation; there were no significant statistical differences.

Discussion

In recent years, there have been many studies comparing TCI with volatile agents because TCI is a new model that has benefit for constant plasma concentration especially when used with propofol. The benefits include PONV prophylaxis, reducing air pollution, and suitable to use with patients with history or family history of malignant hyperthermia. In the present study, we studied laparoscopic cholecystectomy under propofol with TCI compared with volatile agents both sevoflurane and desflurane in terms of PONV and extubation time.

High incidence of PONV was reported after laparoscopic cholecystectomy, 50 to 70% after first 24 hours of surgery[18]. One meta-analysis reviewed nine RCTs showed dexamethasone combined with other antiemetics were significantly better than single antiemetics for prevent PONV[19]. The wound dehiscence, surgical wound bleeding, pulmonary aspiration, dehydration, or electrolyte imbalance could happen after severe PONV[20]. Propofol has the antiemetic effect via 5-HT3 antagonists and/or antidopaminergic activity with depressant effect on the chemoreceptor trigger zone and vagal nuclei[4].

Nowadays, day-procedure laparoscopic cholecystectomy (LC) is more popular. One Cochrane Library reviewed anesthetic regimens: including induction agents, airway devices, muscle relaxants, pain, and quality of life of day-procedure LC[21]. PONV is one cause of hospital admission; therefore, PONV prophylaxis by propofol-TCI technique may take the role to achieve the same day-procedure LC and saves the cost of hospital admission[14,17,22].

Our study showed lower PONV in the propofol-TCI group compared with sevoflurane and desflurane like Inonescu et al[9], Suttner et al[14], and Yao et al[16]. In contrast, Erk et al[6] and Stosic et al[13] showed no statistical differences in terms of PONV however both showed lower incidence and earlier recovery rate. This could be attributed to the fact that propofol has antiemetic mechanisms as the discussion above.

Our study also showed that the extubation time had no significant statistical differences as same as the study by Stotic et al[13], however, it was different from Suttner et al[14]. This was probably due to stop propofol later rather than earlier. Anesthesiologists could make a decision to adjust the plasma concentration setting in TCI easier if the patients had BIS monitoring to detect the depth of anesthesia.

In conclusion, laparoscopic cholecystectomy under propofol with TCI is one choice of anesthesia with significantly lower incidence of PONV compared with volatile agents both sevoflurane and desflurane, otherwise no statistical differences in extubation times. Propofol-TCI technique is suggested for laparoscopic and ambulatory surgery.

What is already known on this topic?

Laparoscopic cholecystectomy is worldwide and standard surgery for the cholecystitis. The anesthesiologists always perform the anesthetic technique using volatile agents that are well known for their side effects, which are nausea and vomiting. In addition, the carbon dioxide, which is used in the laparoscopic surgery, also has the effect on nausea/vomiting. The anti-nausea/vomiting drug may not adequate to relieve the symptoms, lead to longer hospital stay of these patients.

What this study adds?

Nowadays, ambulatory surgery is more popular for laparoscopic cholecytectomy. The present study was to examine the using target-controlled infusion of propofol and examine the incidence of nausea/vomiting, and if this anesthetic technique was the same standard as the volatile technique or better. The result was the incidence of nausea/vomiting decreased, while the anesthetic time was the same. The shorten hospital stay of these patients may save the costs of treatment.

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Potential conflicts of interest

None.

References

1. Hug CC Jr, McLeskey CH, Nahrwold ML, Roizen MF, Stanley TH, Thisted RA, et al. Hemodynamic effects of propofol: data from over 25,000 patients. Anesth Analg 1993; 77 (4 Suppl): S21-9.
2. Vuyk J. Pharmacokinetic and pharmacodynamic interactions between opioids and propofol. J Clin

Anesth 1997; 9 (6 Suppl): 23S-6S.
3. Leslie K, Clavisi O, Hargrove J. Target-controlled infusion versus manually-controlled infusion of propofol for general anaesthesia or sedation in adults. Anesth Analg 2008; 107: 2089.
4. Tramer M, Moore A, McQuay H. Propofol anaesthesia and postoperative nausea and vomiting: quantitative systematic review of randomized controlled studies. Br J Anaesth 1997; 78: 247-55.
5. Clarke KW. Desflurane and sevoflurane. New volatile anesthetic agents. Vet Clin North Am Small Anim Pract 1999; 29: 793-810, viii.
6. Erk G, Erdogan G, Sahin F, Taspinar V, Dikmen B. Anesthesia for laparoscopic cholecystectomy: comparative evaluation--desflurane/sevoflurane vs. propofol. Middle East J Anaesthesiol 2007; 19: 553-62.
7. Frölich MA, Dennis DM, Shuster JA, Melker RJ. Precision and bias of target controlled propofol infusion for sedation. Br J Anaesth 2005; 94: 434-7.
8. Geng Z, Shan G, Song L, Xu X, Wu X. Target-controlled infusions of remifentanil and propofol during laparoscopic cholecystectomy. Beijing Da Xue Xue Bao 2003; 35: 549-52.
9. Ionescu D, Margarit S, Vlad L, Iancu C, Alexe A, Deac D, et al. TIVA-TCI (Total IntraVenous Anesthesia-Target Controlled Infusion) versus isoflurane anesthesia for laparoscopic cholecystectomy. Postoperative nausea and vomiting, and patient satisfaction. Chirurgia (Bucur) 2009; 104: 167-72.
10. Los GJ, Lauwers MH, Van Lersberghe C, Camu F. Influence of sufentanil on propofol anesthesia using a target controlled infusion system. Acta Anaesthesiol Belg 1995; 46: 153-9.
11. Nonaka A, Suzuki S, Nagamine N, Furuya A, Abe F. Postoperative nausea and vomiting after laparoscopic cholecystectomy under total intravenous anesthesia using propofol combined with fentanyl or pentazocine. Masui 2007; 56: 1343-6.
12. Stevanovic PD, Petrova G, Miljkovic B, Scepanovic R, Perunovic R, Stojanovic D, et al. Low fresh gas flow balanced anesthesia versus target controlled intravenous infusion anesthesia in laparoscopic cholecystectomy: a cost-minimization analysis. Clin Ther 2008; 30: 1714-25.
13. Stosic B, Stojanovic M, Jankovic R, Radojkovic M, Ignjatovic N. Implications of anesthetic techniques on patients' recovery in laparoscopic cholecystectomy. Vojnosanit Pregl 2009; 66: 421-6.
14. Suttner S, Boldt J, Schmidt C, Piper S, Kumle B. Cost analysis of target-controlled infusion-based anesthesia compared with standard anesthesia regimens. Anesth Analg 1999; 88: 77-82.
15. Takizawa D, Hiraoka H, Sato E, Aso T, Aso C, Kunimoto F, et al. The effect of gynecologic laparoscopy on propofol concentrations administered by the target-controlled infusion system. J Anesth 2006; 20: 57-9.
16. Yao XH, Zhou P, Xiao ZK, Wang B, Chen CY, Qing ZH, et al. Comparison of target controlled propofol infusion and sevoflurane inhalational anesthesia in laparoscopic cholecystectomy. Nan Fang Yi Ke Da Xue Xue Bao 2007; 27: 1280-1, 1284.
17. Fombeur PO, Tilleul PR, Beaussier MJ, Lorente C, Yazid L, Lienhart AH. Cost-effectiveness of propofol anesthesia using target-controlled infusion compared with a standard regimen using desflurane. Am J Health Syst Pharm 2002; 59: 1344-50.
18. Fujii Y. Management of postoperative nausea and vomiting in patients undergoing laparoscopic cholecystectomy. Surg Endosc 2011; 25: 691-5.
19. Si XY, Wu LP, Li XD, Li B, Zhou YM. Dexamethasone combined with other antiemetics for prophylaxis after laparoscopic cholecystectomy. Asian J Surg 2015; 38: 21-7.
20. Rose JB, Watcha MF. Postoperative nausea and vomiting in paediatric patients. Br J Anaesth 1999; 83: 104-17.
21. Vaughan J, Nagendran M, Cooper J, Davidson BR, Gurusamy KS. Anaesthetic regimens for day-procedure laparoscopic cholecystectomy. Cochrane Database Syst Rev 2014; 1: CD009784.
22. Parra-Sanchez I, Abdallah R, You J, Fu AZ, Grady M, Cummings K III, et al. A time-motion economic analysis of postoperative nausea and vomiting in ambulatory surgery. Can J Anaesth 2012; 59: 366-75.

การดมสลบแบบให้ยา propofol แบบหยดทางหลอดเลือดโดยเครื่องควบคุมเปรียบเทียบกับแบบดมสลบไอระเหยในผู้ป่วยที่มาผ่าตัดถุงน้ำดีแบบส่องกล้อง

สุมิตรา ประเทพ, ศศิธร มหัทธโนบล, วิรัตน์ วศินวงศ์

ภูมิหลัง: *การให้ยาแบบหยอดทางหลอดเลือดโดยเครื่องควบคุม (target-controlled infusion, TCI) มีพัฒนาการมาจากการให้ยาแบบหยอดทางหลอดเลือดแบบควบคุมเอง มีความนิยมเพิ่มมากขึ้นในปัจจุบันนี้โดยเฉพาะการผ่าตัดแบบส่องกล้อง เมื่อเลือกใช้ยา propofol โดยใช้เครื่องควบคุมสามารถลดอุบัติการณ์คลื่นไส้อาเจียนได้*

วัตถุประสงค์: *เพื่อเปรียบเทียบวิธีการดมยาสลบระหว่างการผ่าตัดถุงน้ำดีโดยการส่องกล้องโดยการให้ยา propofol แบบหยอดทางหลอดเลือดโดยเครื่องควบคุม เปรียบเทียบกับการให้ยา propofol แบบหยอดทางหลอดเลือดแบบควบคุมเองและการดมยาแบบแก๊สดมสลบ สามารถลดอาการคลื่นไส้อาเจียนและลดระยะเวลาการถอดท่อหายใจหลังผ่าตัด*

วัสดุและวิธีการ: *การศึกษานี้เป็นการศึกษาเชิงทดลองแบบสุ่มและมีกลุ่มควบคุม ได้ผ่านการพิจารณาจริยธรรมของคณะกรรมการวิจัยและจริยธรรมวิจัย และผู้ป่วยได้ลงลายมือชื่อยินยอมเข้าร่วมการศึกษา โดยศึกษาในผู้ป่วยที่มาผ่าตัดถุงน้ำดีแบบส่องกล้องแบบไม่ฉุกเฉินด้วยวิธีระงับความรู้สึกแบบทั้งตัวจำนวน 75 ราย American Society of Anesthesiologists (ASA) physical status 1 ถึง 3 แบ่งกลุ่มผู้ป่วยออกเป็น 3 กลุ่ม ผู้ป่วยได้รับยา propofol ที่ความเข้มข้นในเลือด 6 ไมโครกรัม/มิลลิลิตร ในกลุ่ม P หรือ 1-2 มิลลิกรัม/กิโลกรัม ในกลุ่ม S และ กลุ่ม D ยา fentanyl 2 ไมโครกรัม/กิโลกรัม และยา vecuronium 0.1 มิลลิกรัม/กิโลกรัม ตามด้วยยา propofol 2-5 ไมโครกรัม/มิลลิลิตร ในกลุ่ม P, sevoflurane 0.5-3% ในกลุ่ม S และ desflurane 2-6% ในกลุ่ม D*

ผลการศึกษา: *อุบัติการณ์การเกิดอาการคลื่นไส้อาเจียนน้อยที่สุดในกลุ่ม P ทั้งที่ห้องพักฟื้น ($p<0.01$) และหอผู้ป่วย ($p = 0.01$) เวลาการถอดท่อหายใจในกลุ่ม P 11.17±1.19 นาที กลุ่ม D 13.96±1.17 นาที และกลุ่ม S 11.75±1.34 นาที ($p = 0.25$) ปริมาณยา fentanyl และสารน้ำไม่มีความแตกต่างกันอย่างมีนัยสำคัญทางสถิติ $p = 0.38$ และ 0.05 ตามลำดับ*

สรุป: *วิธีการดมยาสลบโดยให้ยา propofol แบบหยอดทางหลอดเลือดโดยเครื่องควบคุมเป็นตัวเลือกหนึ่งในการดมยาสลบในผู้ป่วยที่มารับการผ่าตัดถุงน้ำดีด้วยการส่องกล้อง เนื่องด้วยอุบัติการณ์คลื่นไส้อาเจียนต่ำและเวลาการถอดท่อหายใจ ไม่แตกต่างจากการใช้ยาดมสลบไอระเหย seveoflurane หรือ desflurane เหมาะสำหรับผู้ป่วยที่มาผ่าตัดถุงน้ำดีด้วยการส่องกล้องแบบผู้ป่วยนอก*