Post-operative Nausea and Vomiting in Out-Patient Gynecologic Laparoscopy : A Comparison of Thiopental - Nitrous Oxide, Propofol - Nitrous Oxide and Total Intravenous Anesthesia Using Propofol

LAKSAMEE CHANVEJ, M.D.*, SIRIKUL KIJSIRIKUL, M.D.**,
PARAMEE THONGSUKSAI, M.D.***, LAEAD NAHEEM, RN*

Abstract

An intravenous anesthetic drug, propofol was considered to pose antiemetic action. A randomized controlled trial was conducted to evaluate whether propofol could effectively reduce post-operative nausea and vomiting (PONV) compared to thiopental - nitrous oxide (N_2O). One-hundred and eight patients undergoing outpatient gynecologic laparoscopy were assigned to receive 3 techniques of anesthesia; thiopental-N_2O (T/N), propofol-N_2O (P/N) and total intravenous anesthesia (TIVA) using propofol (P/P). The results showed that in the early period (0-5 hours), post-operative nausea in T/N, P/N and P/P groups was 72 per cent, 44 per cent and 31 per cent, respectively (P = 0.002), and post-operative vomiting was 58 per cent, 36 per cent and 11 per cent respectively (P = 0.00014). Patients in the P/N and P/P groups experienced nausea less frequently than the T/N group [relative risk (RR) = 0.62, (95% CI 0.41-0.93) and RR = 0.42 (0.25-0.72) respectively]. Patients in the P/N and P/P groups experienced vomiting less frequently than the T/N group [RR = 0.62 (0.37-1.04) and RR = 0.19 (0.07-0.5) respectively]. Two patients in the T/N group were admitted because of severe nausea and vomiting. In conclusion, TIVA using propofol and propofol-N_2O anesthesia can significantly reduce the incidence of PONV in the early period. Concerning the economic crisis of the country as well as the quality of care, propofol- N_2O would be the most appropriate anesthetic of choice.

Key word : Propofol, Thiopental, Nitrous Oxide, Outpatient Gynecologic Laparoscopy, Post-operative Nausea and Vomiting

**CHANVEJ L, KIJSIRIKUL S,
THONGSUKSAI P, NAHEEM L
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* Department of Anesthesiology, Faculty of Medicine, Prince of Songkla University, Songkhla 90110,
** Department of Anesthesiology, Rajvithi Hospital, Bangkok 10400,
*** Department of Pathology, Faculty of Medicine, Prince of Songkla University, Songkhla 90110, Thailand.

Post-operative nausea and vomiting (PONV) is a common complication after general anesthesia in an outpatient setting. Although this is a minor morbidity, it has been shown to be one of the main reasons for unplanned overnight admission in outpatients[1]. There are many factors postulated to increase the risk of PONV. Age, sex, day of menstruation cycle[2], history of motion sickness and / or previous history of PONV, and anxiety are patient-related factors[3,4]. Opthalmologic, gynecologic, laparoscopic and duration of procedures are operation-related factors[3-5]. Drugs used in balanced general anaesthesia such as morphine[6,7] and neostigmine[8] have been demonstrated to increase the risk of PONV. Anesthesiologists can help decrease PONV by avoiding gastric distention[9] and selecting the anesthetic agents.

Propofol, an intravenous anesthetic agent, has been claimed to have antiemetic effects[10-12]. Anesthetic techniques using propofol for induction and/or total intravenous (TIVA) anesthesia can lower the risk of PONV compared to conventional drugs[13-17]. We evaluated the effectiveness of propofol in reducing PONV compared to thiopental and N_2O which are conventional anesthetic agents routinely used for induction and maintenance of anesthesia in most of the hospitals in the region.

MATERIAL AND METHOD

Patient allocation

Following the faculty ethics committee approval, written informed consent was obtained from 108 patients who had ASA physical status I or II and scheduled for outpatient gynecologic laparoscopy. By using a computer generated list, the patients were randomly allocated into three groups as follows:

Group I (T/N) : Thiopental was used for induction and N_2O for maintenance

Group II (P/N): Propofol was used for induction and N_2O for maintenance

Group III (P/P): Propofol was used for induction and maintenance (total intravenous anesthesia : TIVA)

Based on the statistical power of 80 per cent, expected incidence of PONV at 20 per cent in propofol anesthesia and 54 per cent in conventional anesthesia, 36 patients were required in each group. Patients with a history of allergy to any trial drug or having contraindication for succinylcholine were excluded. Detailed history of motion sickness, previous history of PONV, anxiety and the date of menstruation to determine the phase of menstrual cycle were obtained.

Anesthetic technique

Without pre-medication, all patients were preoxygenated with 100 per cent oxygen for 3 minutes and advised to note any painful sensation at the IV site during induction. Group I received thiopental at a dose of 5 $mg.kg^{-1}$; groups II and III received propofol 2 $mg.kg^{-1}$ IV. Tracheal intubation was facilitated with succinylcholine at 1 $mg.kg^{-1}$ without manual inflation of the lungs before intubation. Groups I and II were then maintained with 67 per cent N_2O in oxygen; group III was maintained with 100 per cent oxygen and 10 $mg.kg^{-1}.h^{-1}$ propofol IV infusion (by using a syringe pump) immediately after the induction dose. All patients received succinylcholine infusion at a rate of 50-100 $\mu gm.kg^{-1}\ min^{-1}$ and fentanyl at 1-3 $\mu gm.kg^{-1}$ which was given as needed to maintain anesthesia. Positive pressure ventilation was given to maintain normocapnia. The patients were placed in a modified lithotomy position with 10-20° Trendelenburg tilt. The laparoscopic procedure was accomplished by using intraperitoneal CO_2 insufflation. The anesthetic maintenance agents were discontinued at the end of surgery and the patients were extubated after adequate spontaneous respiration with good protective airway reflexes. Any untoward reactions to anesthesia or surgical stimuli such as movement, cough, and hiccup were also recorded.

Assessment of PONV and other side effects

The frequency of nausea and vomiting were recorded by the nurse in charge in the recovery room without any knowledge of the patients' group assignments. Each patient was asked about nausea at the end of each hour. Vomiting which presented as actual expulsion of gastric contents was observed and recorded by the nurse. The patients were observed until discharge from the recovery room or until 5 hours after anesthesia for patients whose admission was unplanned. All data represented PONV in the early period. Severity of vomiting in the early period (0-5 hours post-anesthesia) was graded as mild, moderate, and severe when the patient had 1-2, 3-5 and more than 5 episodes respectively. An antiemetic drug, metoclopramide, was given at a dose of 10 mg IV only

Table 1. Demographic characteristics of patients and operative data.

	T/N (n = 36)	P/N (n = 36)	P/P (n = 36)
Age (yr)	33.5 ± 1.7	33.1 ± 5.1	33.6 ± 5.0
Weight (kg)	49.2 ± 15.9	51.6 ± 11.6	51.7 ± 11.0
Height (cm)	156.6 ± 5.7	155.9 ± 6.2	156.4 ± 5.4
BMI	22.0 ± 2.6	21.8 ± 2.5	21.9 ± 3.2
Menstrual phase (28 day cycle)			
- proliferative (day 5-11)	6	11	9
- ovulation (day 12-16)	14	9	12
- secretory (day 17-28)	10	12	11
- menstruating (day 0-4)	-	1	2
- unknown	6	3	2
History of motion sickness	2	8	5
Previous history of PONV	3	5	3
Anxiety	15	19	17
Type of operation			
- Diagnostic Laparoscopy (DL)	25	30	29
- Laparoscopic Tubal Resection (LTR)	11	6	7
Duration of DL (min)	33.6 ± 9.5	36.2 ± 15.2	31.6 ± 7.8
Duration of LTR (min)	41.8 ± 8.6	37.5 ± 11.6	39.7 ± 14.5
Fentanyl (microgram)	79.0 ± 23.8	85.6 ± 21.0	84.4 ± 20
Succinylcholine (mg)	170.7 ± 42.2	187.4 ± 46.4	175.8 ± 54.7

Value for age, weight, height, body mass index (BMI), duration of operation, dosage of fentanyl and succinylcholine are mean ± S.D.
P = not statistically significant, PONV = Post-operative nausea and vomiting

once if the patient had persistent, severe vomiting or complained of severe feelings of nausea.

Post-operative pain was recorded and treated with IV fentanyl until the patient was able to take oral acetaminophen. The time at which the patient sat up without dizziness and the time the patient was discharged from the recovery room were recorded. The discharge criteria included stable vital signs, satisfactory pain control and no nausea and/or vomiting.

The frequency of nausea and vomiting in the next 24-48 hours was obtained by mailing questionnaires. All patients were informed how to record the symptoms of nausea and vomiting before they went home. Other symptoms including post-operative pain, dizziness, myalgia and time at which the patient was able to eat were also obtained.

Statistical analysis

Analysis of variance and Chi-squared test were used to compare demographic characteristics and operative data among study groups where appropriated. Non-parametric approach was used when the continuous data had unequal variance. A p value less than 0.05 was considered significant. Relative risk with 95 per cent confidence interval for the frequency of nausea and vomiting and other complications were calculated.

RESULTS

There were no significant differences among the groups in demographic characteristics of patients and operative data (Table 1). The incidence of nausea in the early period in T/N, P/N and P/P groups was 26/36 (72%), 16/36 (44%) and 11/36 (31%) respectively (P = 0.002). The incidence of vomiting in T/N, P/N and P/P groups was 21/36 (58%), 13/36 (36%) and 4/36 (11%) respectively (P = 0.00014) (Table 2). The P/P group had a significantly lower risk of nausea (95% CI of relative risk excluded 1) compared to the T/N group and had a lower risk of vomiting compared to both P/N and T/N groups. The P/N group also had a significantly lower risk of vomiting compared to the T/N group, but the risk of nausea was marginally significant (Table 2).

Among the patients who experienced nausea, 62 per cent (16/26) in the T/N group and 75 per cent (12/16) in the P/N group first felt nauseated within the first hour while only 9 per

Table 2. Comparisons of nausea and vomiting in early period (0-5 hours post-anesthesia).

	Group			Relative risk (95% confidence interval)		
	T/N n = 36	P/N n = 36	P/P n = 36	P/N : T/N	P/P : P/N	P/P : T/N
Nausea	26	16	11	0.62 (0.41-0.93)	0.69 (0.37-1.27)	0.42 (0.25-0.72)
Vomiting	21	13	4	0.62 (0.37-1.04)	0.31 (0.11-0.85)	0.19 (0.07-0.5)

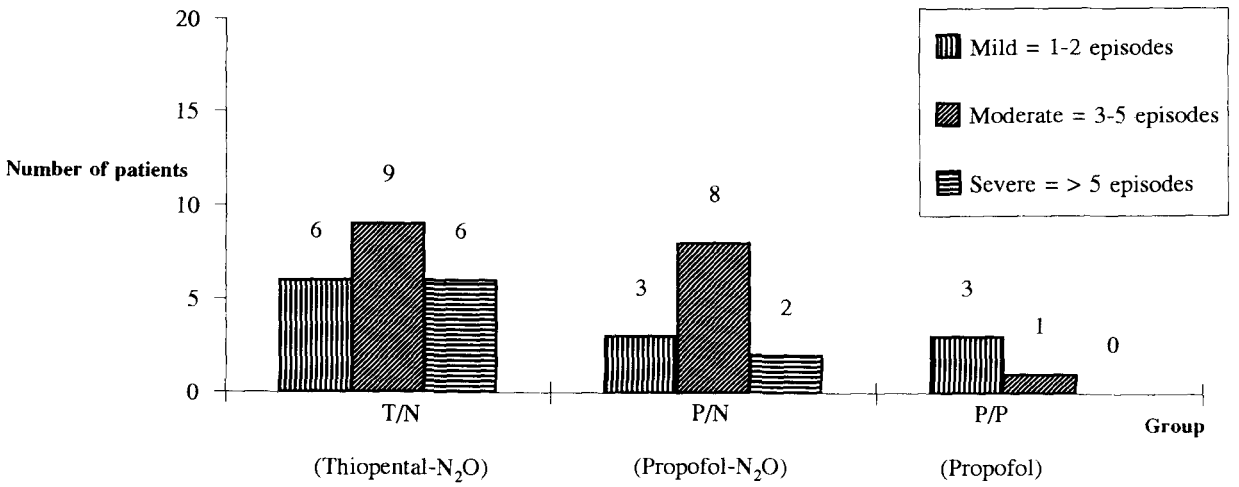

Fig. 1. Severity of vomiting among the groups in early post-anesthetic period (0-5 hour post-anesthesia).

cent (1/11) in the P/P group did (P = 0). Among the patients who had vomiting, 57 per cent (12/21) in the T/N group and 54 per cent (7/13) in the P/N group first vomited within the first hour, whereas, none in the P/P group did.

The distribution of severity of vomiting among the groups in the early period is shown in Fig. 1. Antiemetic treatment was given to 10 patients in the T/N group, 6 in the P/N group and none in the P/P group.

The side effects during the induction, maintenance and recovery periods were not significantly different among the study groups (Table 3). The times required for eye opening and orientation to time, place and person after anesthesia were shorter in the P/N group compared to the P/P and T/N groups (Table 4). Patients in the T/N group took more time to sit up after anesthesia compared to the P/P and P/N groups. Times to discharge from the recovery room were not different among the groups. Thirteen patients had to be admitted overnight for various reasons with only two patients in the T/N group being admitted due to severe PONV.

Patients in the T/N, P/N and P/P groups returned 24, 22, and 27 questionnaires respectively. The frequency of PONV as well as myalgia and post-operative pain in 24-48 hours were not different among the study groups (Table 5). Dizziness in the T/N group was significantly more frequent than the P/P group. The times to first oral intake in T/N, P/P and P/N groups were 8.9 ± 6.9, 4.9 ± 3.7, 6.9 ± 7.1 hours (mean ± SD) respectively. The T/N group significantly delayed the first oral intake compared to the P/P group (P = 0.023).

DISCUSSION

In this study we evaluated whether propofol could reduce the incidence of PONV. Findings of a lower incidence of PONV in the P/N group and P/P group confirmed the effectiveness of the antiemetic effect of propofol when used as an induction agent alone and as a maintenance agent.

The overall PONV incidence in our study was high since it was conducted in conjunction with a gynecologic laparoscopic procedure which is an

Table 3. Comparison of side effects during induction, maintenance and in recovery room.

	T/N	P/N	P/P	Relative risk (95% confidence interval) P/N : T/N	P/P : P/N	P/P : T/N
Induction						
Pain at injection site	9	13	18	1.44 (0.71-2.95)	1.38 (0.8-2.38)	2.0 (1.04-3.84)
Cough, hiccup.	2	1	0	0.5 (0.05-5.27)	-	-
Maintenance						
Cough, hiccup	3	4	2	1.33 (0.32-5.54)	0.5 (0.1-2.56)	0.67 (0.12-3.76)
Movement	6	11	8	1.83 (0.76-4.42)	0.73 (0.33-1.59)	1.33 (0.51-3.46)
Recovery Room						
Pain	16	20	17	1.25 (0.78-2.00)	0.85 (0.54-1.34)	1.06 (0.64-1.76)

Table 4. Comparison of time after anaesthesia.

Time to (min)	T/N	P/N	P/P	P value P/P : P/N	P/P : T/N	P/N : T/N
- Opening eye	2.98 ± 1.72	2.63 ± 1.33	4.47 ± 2.41	0.0007	0.0049	0.369
- Orientation to time, place, person	8.82 ± 8.10	6.78 ± 5.48	12.94 ± 8.91	0	0.05	0.124
- Sit up	139.13 ± 66.41	86.34 ± 48.29	88.00 ± 36.49	0.814	0.0015	0.0006
- Discharge from recovery room	141.00 ± 62.95	118.28 ± 49.87	118.17 ± 39.13	0.992	0.052	0.106

Values are mean ± S.D.

Table 5. Comparison of PONV and other side effects in late period (24-48 hours).

Side effects	T/N (n = 24)	P/N (n = 22)	P/P (n = 27)	Relative risk (95% confidence interval) P/N : T/N	P/P : P/N	P/P : T/N
Nausea	12	6	6	0.57 (0.26-1.26)	0.81 (0.31-2.17)	0.46 (0.2-1.05)
Vomiting	6	4	3	0.73 (0.24-2.24)	1.61 (0.15-2.45)	0.44 (0.12-1.59)
Pain	19	17	21	0.89 (0.56-1.42)	1.24 (0.79-1.92)	1.11 (0.73-1.67)
Dizziness	23	16	11	0.7 (0.45-1.08)	0.69 (0.87-1.27)	0.48 (0.28-0.83)
Myalgia	3	4	4	1.33 (0.32-5.54)	-	1.33 (0.32-5.54)

operation that is highly associated with PONV[3-5]. The findings that propofol induction is associated with a lower incidence of PONV compared to thiopental induction is the same as Myles et al[13], who have reported results in various types of patients and procedures but none in a gynecologic procedure. Using propofol for TIVA as in the P/P group in our study resulted in the lowest incidence of PONV. This was consistent with previous studies [14-17] which demonstrated using propofol for induction and maintenance reduces the incidence of PONV. Since the P/N group had a higher incidence of PONV than the P/P group, this indicates that N_2O during maintenance plays a role in PONV. This PONV potential is similar to many studies [18-20], but not to those of Sengupta et al[21] and Hovorka et al[22].

The results in this study showed that most of the patients in the P/P group first felt nausea or had vomiting in the second hour while most of the patients in the P/N group felt nausea within the first hour which implies that the antiemetic effect lasts longer when using propofol for TIVA. This may be the result of drug accumulation and prolonged elimination half life. Although plasma levels of propofol were not confirmed, the longer time required

for eye opening and orientation to time, place and person in the P/P group compared to the P/N and T/N groups in this study supported this postulation. Although the time to eye opening and orientation in the T/N group and the P/N group were not different, the T/N group took more time before sitting up in the recovery room than the P/N and P/P groups. The hangover from thiopental together with nausea and/or vomiting would be possible reasons for the T/N group to sit up with dizziness. The dizziness which went on after discharge in the T/N group was confirmed by the returned questionnaires. The clear-headed effect of propofol as noted in previous reports[10,23] also explained these findings. These characteristics of propofol may last beyond 24 hours as Heath et al[24] and Millar et al[25] postulated. The time to first oral intake which was sooner in the P/P group compared to the T/N group and the tendency for it to be sooner in the P/N group supported this idea. Nevertheless, in this study no significant difference in PONV in the late period among the groups was found.

The authors concluded that using propofol as an induction agent lowered the incidence of PONV and using it for maintenance resulted in the lowest PONV incidence. At present, TIVA using propofol is widely used in most developed countries. The cost of propofol in Thailand is about ten times higher than thiopental. Considering the economic crisis as well as the quality of care, the use of propofol as an induction agent and N_2O as maintenance would be the most appropriate anesthetic technique for outpatient gynecologic laparoscopy.

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ภาวะคลื่นไส้อาเจียนในผู้ป่วยนอกภายหลังการส่องกล้องทางนรีเวชกรรม โดยการให้ยาสลบไทโอเพนธัล – ไนตรัสออกไซด์ เปรียบเทียบกับโปรโปฟอล – ไนตรัส–ออกไซด์ และเทคนิคการให้ยาสลบทางหลอดเลือดดำโดยใช้โปรโปฟอล

ลักษมี ชาญเวชช์, พ.บ., สิริกุล กิจศิริกุล, พ.บ.**,*
*ปารมี ทองสุกใส, พ.บ.***, ละเอียด นะหีม, พย.บ.**

Propofol เป็นยาสลบที่ให้ทางหลอดเลือดดำที่มีฤทธิ์ต้านอาเจียน คณะผู้วิจัยจึงได้นำมาศึกษาเปรียบเทียบกับ thiopental – nitrous oxide (N_2O) ในการลดภาวะคลื่นไส้อาเจียนหลังผ่าตัด การศึกษาทำในผู้ป่วยนอก 108 คนที่เข้ารับการดมยาสลบเพื่อส่องกล้องทางนรีเวช ผู้ป่วยจะได้รับการสุ่มเพื่อให้ยาสลบ 3 วิธี คือ thiopental – N_2O (T/N), propofol – N_2O (P/N) และเทคนิคการให้ยาสลบทางหลอดเลือดดำ (TIVA) โดยใช้ propofol (P/P) หลังผ่าตัดระยะแรก (0–5 ชั่วโมง) อุบัติการณ์ของคลื่นไส้คือ 72%, 44% และ 31% ตามลำดับ (P = 0.002) อุบัติการณ์ของอาเจียนคือ 58%, 36% และ 11% ตามลำดับ (P = 0.00014) ผู้ป่วยในกลุ่ม P/N และ P/P มีโอกาสคลื่นไส้น้อยกว่ากลุ่ม T/N [RR = 0.62 (95% CI 0.41–0.93) และ RR = 0.42 (0.25–0.72)] ตามลำดับ ผู้ป่วยในกลุ่ม P/N และ P/P มีโอกาสอาเจียนน้อยกว่า T/N [RR = 0.62 (0.37–1.04) และ RR = 0.19 (0.07–0.5)] ตามลำดับ ผู้ป่วย 2 ราย ที่ดมยาสลบด้วย T/N มีอาการคลื่นไส้อาเจียนมากจนต้องรับไว้นอนในโรงพยาบาล ดังนั้นการดมยาสลบโดยใช้ propofol – N_2O และ TIVA โดยใช้ propofol สามารถลดอุบัติการณ์การคลื่นไส้อาเจียนหลังผ่าตัดในระยะแรก เนื่องจาก propofol มีราคาแพงเมื่อคำนึงถึง ราคายาพร้อมกับคุณภาพการดูแลผู้ป่วยการใช้ propofol – N_2O น่าจะเป็นวิธีที่เหมาะสมที่สุด

คำสำคัญ : โปรโปฟอล, ไทโอเพนธัล, ไนตรัสออกไซด์, ภาวะคลื่นไส้อาเจียนหลังผ่าตัด, การส่องกล้องทางนรีเวชแบบผู้ป่วยนอก

ลักษมี ชาญเวชช์, สิริกุล กิจศิริกุล,
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* ภาควิชาวิสัญญีวิทยา, คณะแพทยศาสตร์ มหาวิทยาสงขลานครินทร์, สงขลา 90110
** กลุ่มงานวิสัญญีวิทยา, โรงพยาบาลราชวิถี, กรุงเทพ ฯ 10400
*** ภาควิชาพยาธิวิทยา, คณะแพทยศาสตร์ มหาวิทยาสงขลานครินทร์, สงขลา 90110