Postoperative nausea and vomiting (PONV) is the most frequent side effect after anesthesia occurring in approximately 70% of high-risk inpatients during 24 hours after emergence. It causes dissatisfaction and if in excess, it may result in dehydration along with electrolyte imbalance, suture tension, dehiscence and even aspiration, though rare. Every episode of vomiting may delay discharge from the recovery room by ~20 minutes. Prevention of PONV improves patient satisfaction and provides cost effective care.

The risk factors for PONV can be broadly classified under patient factors and surgical factors along with anesthesia related factors. Patient factors include female gender, obesity, history of nausea and vomiting and genetic predisposition. Surgical factors include types of surgeries and longer duration of surgery. The incidence of PONV after laparoscopic surgery is higher than that after other types of surgeries. As laparoscopic techniques are standardized, so anesthetic drugs and techniques remain the main variable to influence the incidence of PONV. Propofol based anesthesia is known to reduce PONV. Further, coadministration of sevoflurane and propofol to maintain anesthesia has been found to reduce the incidence of PONV compared to sevoflurane alone. However, there are limited studies comparing propofol with a combination of propofol and sevoflurane for the incidence of PONV after laparoscopic surgery. The prospectively randomized, double-blind study was planned to compare propofol and combination of propofol and sevoflurane as maintenance agents for the incidence of PONV. Seventy female patients of 18–60 years, of American Society of Anesthesiologists I or II, undergoing laparoscopic surgery were included. Propofol group (n = 35) included induction with propofol and maintenance with propofol infusion, and propofol + sevoflurane group (n = 35) included induction with propofol and maintenance with a combination of propofol infusion and sevoflurane inhalation. The objectives were to find the incidence of PONV and requirement of rescue antiemetic. In the propofol group, 11 patients (33%) experienced PONV and in the propofol + sevoflurane group, PONV was experienced by 12 patients (38.7%) [0.65]. In the propofol group, 11 patients required ondansetron and out of these 11 patients, 2 patients required metoclopramide. In the propofol + sevoflurane group, Ondansetron was required by 12 patients and 3 patients out of these 12 patients required metoclopramide. In the present study, the incidence of PONV was found to be similar in both groups. So, it can be suggested to add sevoflurane in smaller doses to infusion of propofol for maintenance of anesthesia.

Key words: anesthesia; comparison; females; laparoscopic surgery; maintenance agents; postoperative nausea and vomiting; propofol; sevoflurane

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Prevention and management of postoperative nausea and vomiting (PONV) is a fundamental part of anesthesia. Using sevoflurane and propofol in combination for maintenance of anesthesia has been found to reduce PONV compared to sevoflurane alone. However, there are limited studies comparing propofol with a combination of propofol and sevoflurane for the incidence of PONV after laparoscopic surgery. The prospective, randomized, double-blind study was planned to compare propofol and combination of propofol and sevoflurane as maintenance agents for the incidence of PONV. Seventy female patients of 18–60 years, of American Society of Anesthesiologists I or II, undergoing laparoscopic surgery were included. Propofol group (n = 35) included induction with propofol and maintenance with propofol infusion, and propofol + sevoflurane group (n = 35) included induction with propofol and maintenance with a combination of propofol infusion and sevoflurane inhalation. The objectives were to find the incidence of PONV and requirement of rescue antiemetic. In the propofol group, 11 patients (33%) experienced PONV and in the propofol + sevoflurane group, PONV was experienced by 12 patients (38.7%) [0.65]. In the propofol group, 11 patients required ondansetron and out of these 11 patients, 2 patients required metoclopramide. In the propofol + sevoflurane group, Ondansetron was required by 12 patients and 3 patients out of these 12 patients required metoclopramide. In the present study, the incidence of PONV was found to be similar in both groups. So, it can be suggested to add sevoflurane in smaller doses to infusion of propofol for maintenance of anesthesia.

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SUBJECTS AND METHODS

This study follows the CONsolidated Standards Of Reporting Trials (CONSORT) statement for protocol reporting. Following approval from the Institutional Ethical Committee of Pt. B.D. Sharma University of Health Sciences (approval No. IEC/Th/18/Anst13; December 19, 2019; Additional file 1), the present prospective, randomized, double-blind study was conducted in the Department of Anesthesiology and Critical Care, PGIMS, Rohtak. Seventy female patients of 18–60 years, belonging to the American Society of Anesthesiologists physical status I or II,6 scheduled for elective laparoscopic surgery under general anesthesia were included. The trial was registered at Clinical Trials Registry India (No. CTRI/2019/09/021449; September 30, 2019). Patients with obesity (body mass index > 30 kg/m2), history of nausea and vomiting or motion sickness, history of gastro-esophageal reflux disease, history of antiemetic use in last 2 weeks before surgery including steroids and refusal to participate in the study were excluded.

All the patients were examined during a preoperative visit a day before surgery. Detailed clinical history was taken and examination was done. Required investigations were carried out. Informed and written consent (Additional file 2) was obtained from each patient after explaining the purpose of the study. Patients were kept fasting for 6 hours. Alprazolam 0.25 mg and ranitidine 150 mg was given night before and in the morning 2 hours before surgery with sips of water. Standard monitors were attached. In addition, bispectral index monitoring was instituted in the propofol group. Patients were randomly assigned to one of the two groups, with 35 patients in each group, using a computer-generated sequence of stratified random numbers as follows: propofol group (n = 35): Anesthesia was induced with propofol and propofol infusion was used for maintenance; propofol + sevoflurane group (n = 35): Anesthesia was induced with propofol and combination of sevoflurane and propofol infusion were used for maintenance. After preoxygenation using 100% oxygen for 3 minutes, the induction of anesthesia was done with glycopyrrolate (Neon Laboratories, Mumbai, India), fentanyl (2 μg/kg; Neon Laboratories) and propofol (2 mg/kg; Neon Laboratories). Increments of propofol were given until there was a loss of response to verbal command. After ensuring the ability to mask ventilate, vecuronium (0.1 mg/kg; Neon Laboratories) was administered. Simultaneously, propofol infusion (4–8 mg/kg per hour) in the propofol group and combined propofol (2 mg/kg per hour) and sevoflurane in the propofol + sevoflurane group, along with 67% nitrous oxide in oxygen was commenced. In the propofol group, the propofol infusion rate was titrated to achieve a bispectral index between 40–60. In the propofol + sevoflurane group, the propofol infusion rate was fixed (2 mg/kg per hour) and sevoflurane was titrated to maintain 0.5 minimal alveolar concentration.

After 3 minutes of vecuronium administration, endotracheal intubation was done and ventilation was adjusted to keep end-tidal carbon dioxide between 35–40 mmHg. Carbon dioxide was used to create pneumoperitoneum and abdominal pressures were maintained below 15 mmHg. Ryle’s tube (Arihant Biopharma Co., Pune, India) was inserted to deflate the stomach. The patients in whom laparoscopic surgery was converted to laparotomy were excluded from the analysis. Intravenous ketorolac (Neon Laboratories) 30 mg was administered after the termination of pneumoperitoneum. Propofol infusion and sevoflurane were stopped at the end of surgery. Elective antiemetic was withheld so that we could assess the effect of two anesthetic techniques on the incidence of PONV. Neuromuscular blockade was reversed with glycopyrrolate (0.01 mg/kg) and neostigmine (0.05 mg/kg). After extubation, the patient was shifted to post-anesthesia care unit. Analgesia was provided with diclofenac (Neon Laboratories) 75 mg intravenously every 12 hours. Additional intravenous paracetamol was given at the patient’s request.

Data was recorded for demographic profile, duration of surgery, duration of anesthesia, emesis score, frequency of vomiting, requirement of rescue antiemetic and satisfaction score. Duration of surgery was defined as the time from the incision to the closure of the wound by dressing. Duration of anesthesia was taken as time from induction of anesthesia till time to extubation. PONV was assessed with emesis score (0–3).9 The score was recorded in the recovery room for 2 hours with an interval of 30 minutes and then in the ward for 6 hours, followed by every 6 hours until 24 hours postoperative time. Nausea was defined as subjective and unpleasant sensation associated with an awareness of the urge to vomit. Laboured, spasmodic, rhythmic contractions of the respiratory muscles without the expulsion of gastric contents were defined as retching and vomiting as forceful expulsion of the gastric contents from the mouth. Rescue antiemetic was given if emesis score was ≥ 1. Intravenous ondansetron 4 mg with a lockout interval of 6 hours was given. Metoclopramide 10 mg was given as a secondary rescue antiemetic. The satisfaction score was assessed on a 3-point scale.10 The higher score is, the more satisfied the patients feel.

Researchers have reported the incidence of PONV in patients administered with propofol as 10% as against 39% for the combination of propofol and sevoflurane.11 Taking these as references, the minimum required sample size at 5% level of significance and 85% power was obtained as 31 patients in each group. To compensate for any dropout or exclusion from the study, 35 patients in each group were enrolled. Statistical analysis was performed by the SPSS program for Windows, version 16.0 (SPSS Inc, Chicago, IL, USA). Continuous variables were presented as mean ± standard deviation (SD) and compared using unpaired t-test between groups. Categorical variables were presented as absolute numbers and percentage and were compared using chi-square test. To be statistically significant, P value was taken less than 0.05. The statistical methods of this study were reviewed by the biostatistician of Pt. B.D. Sharma University of Health Sciences.

RESULTS

A total of 70 patients were included in the present study, with 35 patients in each group. The patients in whom laparoscopic surgery was converted to open surgery were excluded from the analysis. There were 2 such patients in the propofol group and 4 in the propofol + sevoflurane group, which made 33 patients in the propofol group and 31 patients in the propofol + sevoflurane group for statistical analysis (Figure 1).
The two groups were comparable with respect to age, weight, body mass index, and American Society of Anesthesiologists physical status. The mean age of patients in the propofol group was 39.87 ± 13.21 years and in the propofol + sevoflurane group it was 40.5 ± 11.33 years (P = 0.87). The mean weight of patients in the propofol group was 60.54 ± 7.66 kg and in the propofol + sevoflurane group was 60.8 ± 8.73 kg (P = 0.89). The mean body mass index was 23.88 ± 2.57 kg/m² in the propofol group and 24.61 ± 3.06 kg/m² in the propofol + sevoflurane group (P = 0.3). Duration of surgery was 67.03 ± 16.79 minutes in the propofol group and 76.41 ± 23.45 minutes in the propofol + sevoflurane group (P = 0.06). Duration of anesthesia was 87.18 ± 17.92 minutes in the propofol group and it was 99.16 ± 24.85 minutes in the propofol + sevoflurane group (P = 0.03).

In the propofol group, 11 patients (33%) experienced PONV and in the propofol + sevoflurane group, PONV was experienced by 12 patients (39%). In the propofol group, 11 patients required ondansetron and out of these 11 patients, 2 patients required metoclopramide. In the propofol + sevoflurane group, Ondansetron was required by 12 patients and 3 patients out of these 12 patients required metoclopramide. A complete response was observed in 22 patients (67%) in the propofol group and 19 patients (61%) in the propofol + sevoflurane group. In the propofol group, 2 patients (6%) had satisfaction score 1, 5 patients (15%) had score 2 and 26 patients (79%) had a satisfaction score 3. In the propofol + sevoflurane group, 2 patients (6%) had satisfaction score 1, 12 patients (39%) had score 2 and 17 patients (55%) had satisfaction score of 3. More patients were completely satisfied in the propofol group (79%) than in the propofol + sevoflurane group (55%); however the difference was not statistically significant (P = 0.09).

**DISCUSSION**

The primary objective was to observe the incidence of PONV. Patients with emesis score > 0 were considered to have PONV. The incidence of PONV in two groups did not show a significant difference. These results of the present study are in accordance with different studies.1,7 Uchinami et al.1 also observed no significant difference in the two groups – propofol and the combination of propofol and sevoflurane (27.8% vs. 33.3%, P = 0.80). Their study included female patients undergoing laparoscopic gynecological surgery. However on the contrary, when the propofol group of the present study was compared, PONV was found to be more in the present study. Similarly, the incidence was found to be higher for the propofol + sevoflurane group in the present study.7 This difference may be due to the fact that these authors used remifentanil whereas in the present study fentanyl was used. A single bolus of 2 µg/kg of fentanyl at the time of anesthetic induction has been found to increase the incidence whereas remifentanil infusion when given intraoperatively does not result in PONV.12

Won et al.7 compared the PONV after thyroidectomy and observed that its incidence was significantly lower with total intravenous anesthesia and combined group as compared to the sevoflurane group (33.9%, 39%, and 64.4%). Also no significant difference was observed in the incidence of PONV between total intravenous anesthesia and combined groups. These authors used propofol via target-controlled infusion whereas in the present study induction of anesthesia was done with 2 mg/kg in both groups and propofol infusion was started at 4–8 mg/kg per hour in the propofol group and at 2 mg/kg per hour in the propofol + sevoflurane group.7

Kawano et al.6 observed the influence of combining propofol and sevoflurane on PONV in patients undergoing laparoscopic gynecological surgery. The incidence was observed as sevoflurane group 62%, propofol alone group 29% and combination group 21%. However, these authors did not compare propofol alone group with combination groups. Rather, they compared both propofol alone and combination groups with the sevoflurane group. Compared with the propofol group, the incidence of PONV was higher in the propofol group in the present study (33.3% vs. 29%) and similarly, this incidence was higher in the combined group in the present study (38.7% vs. 21%).6 The main reason behind this may be the use of remifentanil by these authors whereas in the present study fentanyl was used. Additionally, these authors used air and oxygen whereas in the present study N2O & O2 were used. PONV was increased from 27% without nitrous oxide to 33% with nitrous oxide in a meta-analysis by Fernandez Guisasola et al.13

In the present study, PONV was found to be the same in both groups. Propofol is known to have antiemetic effect. This antiemetic effect was found to be related to a defined plasma concentration range.14 Propofol was used in both groups in the present study. Duration of exposure to volatile agents is the main cause of PONV in the early postoperative period.15 However, sevoflurane was used in smaller doses in the propofol + sevoflurane group, which might be the reason for the similar PONV in the two groups. Additional benefits of sevoflurane include prevention of intraoperative awareness, cardioprotective effects as well as bronchodilator effects.1 It was also observed that the incidence of PONV was maximum in the early postoperative period (0–6 hours) in both groups (P = 0.83) and was negligible thereafter.

The secondary objective of the present study was the requirement of rescue antiemetic. Patients with emesis score > 0 were considered to have PONV and rescue antiemetic was given at emesis score ≥ 1. Hence all the patients who had PONV, were given ondansetron. However, this difference was not observed to be significant. In the propofol group, two patients required metoclopramide and three patients in the propofol + sevoflurane group required metoclopramide. These results are consistent with different studies.1,7 Uchinami et al.1 also
did not observe any difference in the number of patients who required antiemetics (22.2% in the propofol alone group vs. 22.2% in combination group). These authors also did not use antiemetic for prophylaxis.1 Similarly Won et al.7 also did not find any difference in requirement of rescue antiemetic in the propofol group and combined group (11.9% vs. 15.3%). These authors used 10 mg metoclopramide as rescue antiemetic at the patient’s request. However, in the present study rescue antiemetic was given at emesis score ≥ 1.

In females, PONV has been observed three times as compared with males.16 Further, in female patients undergoing laparoscopic surgeries, the incidence of PONV has been reported to be as high as 50–80%.17,18 Though prophylaxis for PONV has been recommended in high risk patients, however, no prophylactic antiemetic was given in the present study to estimate the influence of two techniques in a better way and assess the baseline risk, which would have been masked by prophylaxis. Moreover, prophylactic antiemetic results in an increase in cost and side effects.

No significant difference in complete response was observed in the present study, which is similar to Kawano et al.6 At the end of the study period, the satisfaction score was evaluated. Though more patients showed complete satisfaction in the propofol group (78.8% vs. 54.8%), the difference was not statistically significant (P = 0.09), which is consistent with Won et al.7

Surgery duration was the same in both groups in the present study; however duration of anesthesia was longer in the propofol + sevoflurane group. Duration of anesthesia was taken as the time from induction of anesthesia until extubation. This increased duration in the propofol + sevoflurane group may be due to increased extubation time in the propofol + sevoflurane group.

Though the data was not collected, however, no patient had awareness in the present study. In the propofol group, it might be due to the fact that bispectral index was targeted between 40–60. Moreover, in the propofol + sevoflurane group, sevoflurane must have contributed to this prevention of awareness. Pain is another risk factor for PONV. Appropriate measures were taken to control postoperative pain. Opioids were not used postoperatively; instead, nonsteroidal anti-inflammatory drugs were the mainstay of postoperative pain management.

The present study has a few limitations. Only the combination of propofol infusion and sevoflurane was studied. Other combinations may be investigated for optimal effect. No data were collected regarding awareness and hemodynamic parameters. Cost effectiveness was not evaluated, which is one of the limitations of the study.

In the present study, the incidence of PONV was found to be similar in both groups. So, it can be suggested to add sevoflurane in smaller doses to infusion of propofol for maintenance of anesthesia.

Author contributions
Literature search: TB, SS, KK; case conduction: TB, KK; manuscript writing and editing: TB, SS. All authors read and approved the final manuscript.

Conflicts of interest
None.

References
1.UCHINAMI Y, TAKIKAWA S, TAKASHIMA F, et al. Incidence of postoperative nausea and vomiting after laparoscopic surgeries: a comparison of standard anesthetic technique and propofol infusion. Acta Anaesthesiol Taiwan. 2010;65:379-387.
2. AKKURT BC, TEMIR M, INANOGLU K, et al. 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. Curr Ther Res Clin Exp. 2009;70:94-103.
3. SINGH SK, KUMAR A, MAHAJAN R, KATyal S, MANN S. Comparison of recovery profile for propofol and sevoflurane anesthesia in cases of open cholecystectomy. Anesth Essays Res. 2013;7:386-392.
4. LIM H, Doo AR, Son JS, et al. Effects of intraoperative single bolus fentanyl administration and remifentanil infusion on postoperative nausea and vomiting. Korean J Anesthesiol. 2016;69:51-56.
5. FERNÁNDEZ-GUISASOLA J, GÓMEZ-ARNAU H, CABRERA Y, DEL VALLE SG. Association between nitrous oxide and the incidence of postoperative nausea and vomiting in adults: a systematic review and meta-analysis. Anesthesia. 2010;65:379-387.
6. GIANTJ, Glass PS, HOWELL ST, CANADA AT, Grant AP, Ginsberg B. Determination of plasma concentrations of propofol associated with 50% reduction in postoperative nausea. Anesthesiology. 1997;87:779-784.
7. APTIOL CC, KRANKE P, KATZ MH, et al. Volatile anaesthetics may be the main cause of early but not delayed postoperative vomiting: a randomized controlled trial of factorial design. Br J Anaesth. 2002;88:659-668.
8. GIANT J. Postoperative nausea and vomiting-can it be eliminated? JAMA. 2002;287:1233-1236.
9. SHAHID SI, NAGAREKHA D, HEGADE G, MARUThEESH M. Postoperative nausea and vomiting: a simple yet complex problem. Anesth Essays Res. 2016;10:388-396.
10. SHIM HK, LEE MH, MOON SY, et al. Post-operative nausea and vomiting after gynecologic laparoscopic surgery: comparison between propofol and sevoflurane. Korean J Anesthesiol. 2011;60:36-40.

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Additional files
Additional file 1: Hospital Ethics Approval.
Additional file 2: Informed consent form.