Original Article

Prevention of postoperative nausea and vomiting with a subhypnotic dose of Propofol in patients undergoing lower abdominal surgery: A prospective, randomized, double-blind study

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Abstract

Background: Postoperative nausea and vomiting (PONV) is a common complication after general anesthesia in patients undergoing elective lower abdominal surgery. We aimed to compare the effect of a sub hypnotic dose of Propofol in the prevention of PONV after lower abdominal surgery with that of the conventional antiemetic drug Metoclopramide.

Materials and Methods: In this prospective, randomized, double-blind, placebo-controlled study, 104 patients with American Society of Anesthesiologists (ASA) class I or II status, aged 18–65 years, and undergoing elective lower abdominal surgery were randomized to one of four groups (n = 26 each). The patients in the four groups were administered intravenously Propofol 20 mg (G1), Propofol 30 mg (G2), Metoclopramide 10 mg (G3), and placebo (G4), 15 min before skin closure. All episodes of PONV during the first 24 h after anesthesia were recorded by an investigator who was blinded to treatment assignment.

Results: There were no significant differences between the treatment groups with regard to their gender, age, ASA class, duration of surgery, duration of recovery time and hospital stay, and also body mass index (BMI) ($P > 0.05$). The prevalence of PONV 0-6 h after anesthesia was 23.08% with Propofol 20 mg ($P = 0.005$), 15.38% with Propofol 30 mg ($P = 0.016$), 15.38% with Metoclopramide 10 mg ($P = 0.016$), compared to 30.77% with placebo ($P = 0.005$).

Conclusions: Administration of a subhypnotic dose of Propofol (30 mg) was found to be as effective as 10 mg Metoclopramide in reducing the incidence and severity of PONV in adult patients undergoing elective lower abdominal surgeries under Isoflurane-based anesthesia in the early postoperative period.

Key Words: General anesthesia, lower abdominal surgery, metoclopramide, postoperative nausea and vomiting, Propofol

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Received: 06.01.2013, **Accepted:** 15.01.2014

Access this article online	
Quick Response Code:	Website: www.advbiores.net
	DOI: 10.4103/2277-9175.151239

INTRODUCTION

Postoperative nausea and vomiting (PONV) is one of the most distressing and common side effects of anesthetics and may cause severe discomfort among patients.[1] In addition, PONV can lead to delayed post-anesthesia admission and higher medical costs.[2]

How to cite this article: Naghibi K, Kashefi P, Azarnoush H, Zabihi P. Prevention of postoperative nausea and vomiting with a subhypnotic dose of Propofol in patients undergoing lower abdominal surgery: A prospective, randomized, double-blind study. Adv Biomed Res 2015;4:35.

The incidence of PONV in patients has been reported to be from 20 to 70% after various types of surgeries, when no prophylactic antiemetic is provided.[3-5]

PONV can cause severe discomfort amongst patients and is probably related to several factors, which include age, sex, operation type, and anesthesia-related factors.[6-8] Other factors, including obesity, a history of motion sickness and/or a history of previous postoperative emesis, and also preoperative volume loading may have an important role in PONV.[9-11]

The optimal strategy for preventing PONV remains contentious.[12]

Global prophylaxis for PONV is generally not recommended, although it has been demonstrated to be cost-effective in high-risk patients.[13,14]

PONV occurs frequently in patients undergoing lower abdominal surgeries.[15,16]

With respect to anesthetic agents, nitrous oxide (N_2O) and volatile anesthetics increase the occurrence of PONV, but Propofol is known to have an antiemetic effect.[17-20]

The data on the efficacy of specific antiemetics and their combination are still lacking, so definitive conclusions are difficult to make at present. On the other hand, while the efficacy of Propofol is presently not clear, Metoclopramide, a popular antiemetic for decades, was found to have limited efficacy at the lower traditional dosage.

Thus, the purpose of this study was to compare the number of patients who have symptoms of PONV and the objective degree of PONV which occurs after general anesthesia with Isoflurane and a subhypnotic dose of Propofol at each time period during the post-anesthesia period in patients undergoing elective lower abdominal surgeries.

MATERIALS AND METHODS

One hundred and four American Society of Anesthesiologists (ASA) physical status I and II patients of age 18-65 years and who were scheduled for elective lower abdominal surgery under general anesthesia participated in this randomized double-blinded clinical trial [Figure 1].

The study protocol was approved by Isfahan University of Medical Sciences ethics committee, and all patients gave written informed consent. The study was performed in Alzahra University Hospital in Isfahan in 2009.

Before anesthesia, patients with a risk factor of PONV, or with a prior history of motion sickness or PONV and also administration of an antiemetic before surgery, patients with a history of drug or alcohol abuse, and patients with body mass index (BMI) >30 kg/m^2 were not included.

The patients with any unpredictable condition in surgery or any complication such as severe hypotension [whenever systolic blood pressure (SBP) was less than 70% of baseline] or bleeding more than 10% of total blood volume were excluded.

The sample size was estimated based on a power calculation which showed that at least 26 patients per group were necessary to achieve 80% power to detect a 20% difference between the four groups in the visual analog scale (VAS) scoring with an α equal to 0.05.

Patients were randomly allocated into one of four groups (Propofol 20 mg (G1), Propofol 30 mg (G2), Metoclopramide 10 mg (G3), or isotonic saline as a placebo (G4)) using sealed envelopes, with 26 patients in each group.

The baseline heart rate (HR), SBP, diastolic blood pressure (DBP), and mean arterial pressure (MAP), and also SaO_2 were recorded every 15 min during the entire anesthesia period and also every 15 min during the recovery period. No premedication was given to the patients.

In all groups, induction of anesthesia was carried out with sodium thiopental 6 mg/kg, Fentanyl 2 mic/kg, Morphine 0.15 mg/kg, and Atracurium 0.6 mg/kg and then trachea was intubated. Maintenance of anesthesia was performed with 50% N_2O and O_2, and also, 1 minimum alveolar concentration (MAC) of Isoflurane with controlled ventilation. Mechanically controlled ventilation was adjusted to maintain an end-tidal CO_2 concentration between 35 and 45 mm Hg throughout the surgery.

Fifteen minutes before the end of surgery, patients were administered either 20 mg Propofol (G1), 30 mg Propofol (G2), 10 mg Metoclopramide (G3), or the same volume of isotonic saline as placebo (G4). The injected drugs were prepared in identical syringes by a researcher not otherwise involved in this study.

At the end of the surgery, the residual of neuromuscular block was reversed with a mixture of 0.02 mg/kg atropine and 0.04 mg/kg of neostigmine.

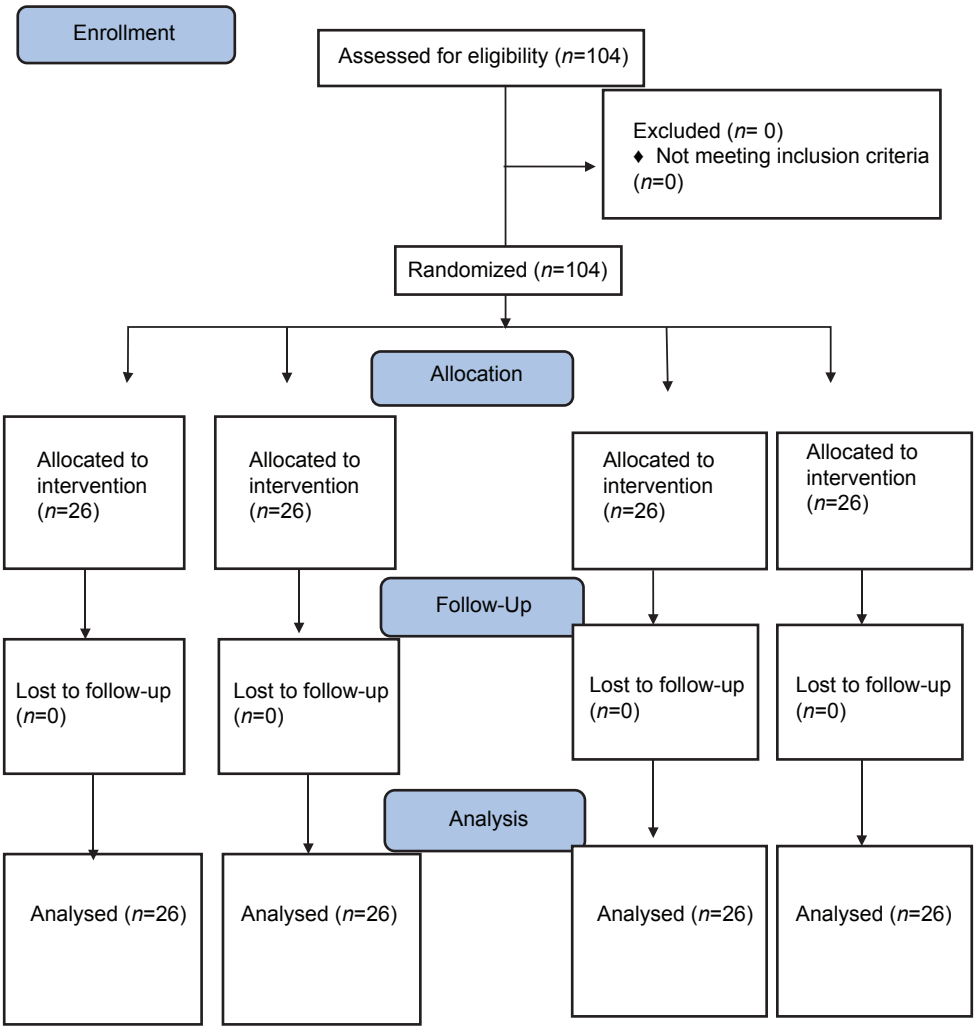

Figure 1: CONSORT Flow chart 1

The incidence and severity of PONV and the side effects of the antiemetic during the first 24- h period after the surgery were recorded. These variables were assessed by the investigators unaware of the group identities and subdivided into three time periods, 0-6 h, 6-12 h, and 12-24 h, postoperatively. Duration of surgery (min) and also duration of the recovery period (min) were recorded.

Nausea was defined as a subjectively unpleasant sensation associated with an awareness of the urge to vomit. Severity of nausea was determined using verbally voted scores, wherein mild was defined as a score of 1-3, moderate as a score of 4-6, and severe as a score of 7-10.[21]

Vomiting was defined as the forceful expulsion of the gastric content from the mouth and was treated with a single stat dose of Metoclopramide 0.15 mg/kg body weight intravenously.

The baseline HR, SBP, DBP, and MAP, and also SaO_2 were recorded every 15 min throughout the surgery and also in the recovery room. Duration of surgery (the time from the start of surgery to the closure of the wound by dressing) and also duration of recovery stay [the time from arriving to the post-anesthesia care unit (PACU) to discharge from there] were recorded.

If patients were awake and had no PONV or hemodynamic instability, they were discharged from PACU.

The collected data were entered into a computer and analyzed by SPSS version 20 software. Data are presented as mean ± SD or number (percent). Data such as age, weight, anesthesia time, and recovery time were compared using Student's *t*-test; sex distribution and ASA physical status were measured by using χ^2-test or Fisher's exact test if needed. The trend and change of HR, SBP, DBP, and MAP during different time periods were analyzed by repeated measures analysis of variance (ANOVA) test. $P < 0.05$ was considered statistically significant.

For multiple comparisons among means, ANOVA with Fisher's protected least-significant difference test. In addition, the difference between these trends was analyzed by paired *t*-tests.

RESULTS

The four groups of patients were comparable with respect to sex, mean age, weight, height, male to female ratio, ASA physical status, and duration of surgery and also recovery time [Table 1].

The incidence of complete response (% of patients with no PONV) in the four groups was 76.92, 84.61, 84.61, and 69.23%, respectively, during the first 6 h ($P \leq 0.05$).

During the first 6-h period after emergence, the incidence of complete response was significantly higher, and the severity of nausea and the use of rescue antiemetic medication were significantly lower in the Propofol 30 mg and also Metoclopramide 10 mg groups compared with the other two groups, but these effects were not observed during the other periods [Table 2].

The mean age of patients in groups 1–4 was 46.7 ± 6.4, 49.4 ± 8.2, 42.3 ± 6.7, and 47.4 ± 5.3 years, respectively, and results of the *t*-test showed that there was no significant difference between them ($P > 0.05$).

All the study groups were comparable with respect to their demographic data. The baseline values of all groups showed no significant differences ($P < 0.05$).

According to the repeated measures ANOVA, the mean changes of HR, SaO_2, SBP, DBP, and MAP during the anesthesia period and recovery time in all the groups were not statistically significant ($P > 0.05$)[Table 3].

Table 1: Patients characteristics, duration of surgery, hospital stay, and calculated risks for PONV

Variable	G1 (20 mg Propofol, *n*=26)	G2 (30 mg Propofol *n*=26)	G3 (10 mg Metoclopramide *n*=26)	G4 (placebo, *n*=26)	*P*
Sex (M/F)	8/18	11/15	9/17	10/16	>0.05
Age (years)	46.7±6.4	49.4±8.2	42.3±6.7	47.4±5.3	>0.05
ASA (I/II)	21/5	19/7	20/6	22/4	>0.05
Weight (kg)	68±5.2	71.2±12.4	70±13	64±6.2	>0.05
Height (cm)	168±13	172±9	163±12	161±5.5	>0.05
Duration of surgery (min)	96±25	110±35	106±14	98±22	>0.05
Duration of hospital stay (days)	1.8±0.6	2.1±0.8	1.6±0.4	1.4±0.3	>0.05
Calculated risk for PONV (%)	23.08	15.38	15.38	30.77	<0.05

Values are presented as mean±SD or the number of patients. No significant difference was noted between the four groups except for the calculated risk for PONV.
M/F: Male/Female, ASA: American society of anesthesiologists, PONV: Postoperative nausea and vomiting

Table 2: Incidence and severity of nausea and vomiting and requirements for antiemetic treatment

Variable	G1 (*n*=26)	G2 (*n*=26)	G3 (*n*=26)	G4 (*n*=26)	*P* value
0–6 h postoperative complete response	20 (76.92%)	22 (84.61%)	22 (84.61%)	18 (69.23%)	0.033*
Nausea	6 (23.08%)	4 (15.39%)	4 (15.39%)	8 (30.77%)	0.042*
Mild/moderate/severe	2/1/3	2/2/0	2/1/1	2/2/4	
Vomiting	6 (23.08%)	4 (15.39%)	4 (15.39%)	8 (30.77%)	0.042*
Rescue antiemetics	4	2	2	6	0.032*
0–6 hours postoperative					
Rescue antiemetics	8	7	7	8	0.923
6–24 h postoperative					
Side effects of antiemetics (headache, dizziness, drowsiness)	0	0	0	0	1.000
The mean total dose of antiemetic used after the surgery	5.2±2.1	5±0.9	6±1.8	12±4.6	0.042*

Values are presented as number (%). *P<0.05

Table 3: Intraoperative maximum mean arterial blood pressure and heart rate changes, blood loss, morphine use, and PACU stay in the four groups

Variable	G1 (*n*=26)	G2 (*n*=26)	G3 (*n*=26)	G4 (*n*=26)	*P* value
Maximum heart rate changes (rate/min)	+20±4.6	+24±6.8	+18±6.2	+16±7	>0.05
Maximum mean arterial blood pressure changes (mmHg)	−15.3±7.5	−12.4±4.9	−8±4.5	−14±6.4	>0.05
Blood loss	500±130	580±95	450±55	500±75	>0.05
Total morphine use 6 h postoperatively (mg)	10.2±4.3	10.6±0.9	12±4.6	9.6±5.2	>0.05
Total morphine use 6–24 h postoperatively (mg)	15.45±4.3	17.2±6.5	18±5.6	14.5±5.8	>0.05
PACU stay (min)	126±12	75±6	95±15	65±20	>0.05

Values are presented as mean±SD or number (%). PACU: Post-anesthesia care unit

The incidence of postoperative complications such as hypotension, hypertension, tachycardia, or bradycardia, and shivering was very low (two cases of shivering in group 3, two cases of hypotension in group 1, and 1 case of bradycardia in group 1) and the statistical analysis was not possible.

DISCUSSION

Lower abdominal surgeries are associated with a relatively higher incidence of PONV. It can be problematic, particularly after lower abdominal surgeries since it can lead to complications such as wound dehiscence, prolonged recovery stay and also prolonged hospital stay, and moreover, increased cost.[22] Therefore, PONV is the anesthetic complication of greatest concern for patients and continues to be a significant concern for anesthesiologists.[5]

Propofol is a short-acting intravenous hypnotic agent used for induction and maintenance of general anesthesia and sedation for surgical operation and mechanical ventilation in adults.[23] Furthermore, Propofol has been reported to be an effective antiemetic in patients who had undergone various surgeries.[24-27] However, the optimal dose of Propofol to reduce the PONV is debatable and has not been established. Hence, more studies are necessary to determine the drugs and their doses that should be selected.

A number of well-designed trials with controversial results about the prevention of PONV with a subhypnotic dose of Propofol have been published.[28-31] Shinn *et al*., in a randomized clinical trial of 38 patients who underwent gynecologic laparoscopic surgery, reported that the incidence of PONV during the first 24 h postoperatively in the case of Propofol was significantly lower than that with Sevoflurane, and this corresponds to the results of the present study which have established the antiemetic effect of Propofol. But while the number of patients with PONV within 1 h postoperatively in the case of Propofol was significantly less than with Sevoflurane, there were differences in the number of patients with symptoms of PONV from 1 to 6 h and also from 6 to 24 h postoperatively.[32]

In the present study, the dose of Propofol used was decided by referring to previous studies which reported that a subhypnotic dose of 30 mg of Propofol is required to prevent PONV during the 24 h after surgeries with Isoflurane anesthesia.[33-35]

A systemic review of 84 randomized controlled trials that compared Propofol with inhalational agents showed that the preventative effects of Propofol on PONV were significant only in high-risk patients during early PONV (<6 h).[36,38] Apfel *et al*. concluded in a randomized controlled study of 1180 patients at high risk for PONV that the risk factors of late PONV (2-24 h) and early PONV (2 h) were different.[37] Although we found a trend toward a greater complete response in the 30 mg Propofol group, this was significant only during early PONV (<6 h), which is consistent with the result of Apfel *et al*. on the prevention of PONV in patients after Propofol-based anesthesia in total intravenous anesthesia (TIVA)[38] Therefore, appropriate prophylactic antiemetic treatment should be considered.

The results of the present study show that a subhypnotic dose of Propofol (30 mg) reduces the incidence and severity of nausea in patients who had undergone lower abdominal surgeries [Table 2]. However, the use of traditional antiemetics is limited by their side effects, which include dysphoric and extrapyramidal symptoms.

In conclusion, we found that 30 mg propofol was effective in preventing PONV in patients who had undergone elective lower abdominal surgeries with Isoflurane-based anesthesia, especially during the first 6 h after the surgery.

The limitation of this study was the small sample size and the fact that we followed patients only for 24 h postoperatively; however, the findings seem particularly robust in spite of this.

To conclude, we suggest similar studies comparing the effects of type of anesthesia or other types of surgeries and different injection time periods of subhypnotic dose of propofol on PONV. On the other hand, postoperative analgesia with opioids is associated with an incidence of PONV in over 30% of patients. As PONV management in patients with preoperative narcotic dependency or acute opioid tolerance is challenging,[39] it requires further studies.

ACKNOWLEDGMENTS

The authors would like to express their gratitude to all those from Alzahra University Hospital who helped us complete this research. Furthermore, our special thanks are extended to the staff of post-anesthesia care unit and the surgery ward for their warm assistance with the collection of our data.

The authors have no funding or support to report.

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Source of Support: Nil, **Conflict of Interest:** None declared.