

Frequency of Postoperative Nausea and Vomiting after General Anesthesia in a Tertiary Care Hospital: A Comparison of Palonosetron and Dexamethasone

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ABSTRACT

Introduction: Postoperative nausea and vomiting (PONV) is an unpleasant sensation often described as worse than postoperative pain. Various drugs, including scopolamine, gabapentin, dexamethasone, metoclopramide, promethazine, haloperidol, and serotonin receptor antagonists, have been used for prophylaxis of PONV, but none has been 100% efficacious. We hereby try to compare the effects of palonosetron and dexamethasone on the frequency of PONV.

Aims and objectives: The aim of our study was to compare the frequency of PONV with palonosetron and dexamethasone in patients undergoing elective laparoscopic cholecystectomy surgery under general anesthesia.

Material and methods: In this prospective, randomized, double-blind study, 50 patients scheduled for laparoscopic cholecystectomy were randomized into two groups receiving 8 mg dexamethasone or 0.075 mg palonosetron. The frequency of PONV in the two groups was compared.

Results: Statistical analysis was done using SPSS version 20 (SPSS Inc., Chicago, Illinois, USA). The patients in the two groups were comparable in terms of mean age, body mass index, and gender distribution. At 4, 8, and 12 hours, the incidence of PONV was significantly less in patients receiving palonosetron than those receiving dexamethasone ($p = 0.007, 0.001, 0.001$, respectively).

Conclusion: We can conclude from the present study that 0.075 mg palonosetron is more effective than 8 mg dexamethasone to reduce the incidence of PONV after laparoscopic cholecystectomy.

Keywords: Dexamethasone, Laparoscopic cholecystectomy, Palonosetron, Postoperative nausea and vomiting.

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INTRODUCTION

Since the inception of general anesthesia, postoperative nausea and vomiting (PONV) remains an important complication after surgery for which no complete solution is available till date. PONV is an unpleasant sensation, which a patient often describes as worse than postoperative pain. Laparoscopic surgeries are associated with high incidence of PONV. The incidence of PONV in the surgical population ranges from 30 to 40%. In high-risk patients, it is up to 80%.¹

Various drugs have been used for prophylaxis of PONV, including scopolamine, gabapentin, dexamethasone, metoclopramide, promethazine, haloperidol, and 5-hydroxytryptamine 3 (5-HT₃) receptor antagonists.² Due to enhanced safety profile compared to other antiemetic agents, 5-HT₃ antagonists have gained more popularity in managing PONV. Their actions involve both central and peripheral mechanisms in control of nausea and vomiting. Centrally, they bind competitively and selectively to serotonin receptors in the chemoreceptor trigger zone (CTZ) of the central nervous system. CTZ sends projection to the vomiting center located in the lateral reticular formation of medulla oblongata. They also block receptors in the gastrointestinal tract, which prevents the action of serotonin and inhibits emetic symptoms.³

Commonly used 5-HT₃ antagonists are ondansetron, granisetron, dolasetron, and palonosetron. The main difference among these agents is related to their chemical structures, receptor affinity, and pharmacokinetic profile.⁴ Palonosetron, a newer 5-HT₃ receptor antagonist, has recently been introduced and has a longer

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half-life of around 40 hours and a better safety profile.⁵ It has not been associated with significant QT interval prolongation, an effect observed with other 5-HT₃ receptor antagonists.⁶

Dexamethasone has a central antiemetic action through the activation of glucocorticoid receptor in nuclei tractus solitarius in medulla. Dexamethasone has low cost and prolonged biological half-life of 36-48 hours.⁷

There is limited literature comparing the efficacy of palonosetron and dexamethasone. Therefore, we hereby make an attempt to compare the effect of palonosetron and dexamethasone on the frequency of PONV in elective laparoscopic cholecystectomy surgeries under general anesthesia.

MATERIALS AND METHODS

A prospective, randomized, double-blind study was conducted in 50 patients of either sex aged 18–60 years, belonging to grades 1 and 2 of American Society of Anesthesiologists undergoing elective laparoscopic cholecystectomy under general anesthesia after obtaining ethical clearance from the Institutional Ethical Committee. A written informed consent was obtained from the participants. Exclusion criteria were pregnant females, patients with history of nausea, vomiting, or retching in 24 hours before anesthesia, antiemetic therapy in 24 hours before surgery, or known hypersensitivity or contraindications to study drugs.

Group size of the study was determined by considering alpha error of 0.05 and power of study 80%. The number needed to study was calculated to be 22 in each group. Considering 8–10% dropout rate, sample size was increased to 50 with 25 patients in each group. The study patients were divided into two groups based on computer-generated random numbers, sealed in 50 envelopes. The slip was taken out by the consultant on duty not involved in the study, and the drug was prepared according to the coded slip. Group A ($n = 25$) received 8 mg of inj. dexamethasone made into 5 mL with normal saline i.v. Group B ($n = 25$) received 0.075 mg of inj. palonosetron made into 5 mL with normal saline i.v. Both the patient and the observer were unaware of the drug solution injected.

Preanesthetic assessment was carried out 1 day before surgery. Details pertaining to patients' clinical history, general physical and systemic examinations, and basic routine investigations like hemoglobin, total and differential leukocyte count, routine urine, blood urea nitrogen, serum creatinine, bleeding time, clotting time, and electrocardiogram (ECG) were noted. All patients were kept fasting overnight for at least 6 hours. All patients were given 0.5 mg alprazolam orally on night before surgery and on early morning before surgery. On arrival of the patient in operating room, all the monitors were attached—noninvasive blood pressure, heart rate, ECG, and arterial oxygen saturation—and the vitals were recorded. Intravenous cannulation in one of the peripheral veins with a 20 G cannula was established and i.v. crystalloids infusion was started. Glycopyrrolate (0.2 mg) and butorphanol (1 mg) were given for premedication. Preoxygenation with 100% O₂ was done for 3 minutes, followed by induction using inj. propofol (2 mg/kg) and inj. succinylcholine (1 mg/kg) intravenously. Intubation was done with appropriate size cuffed oral endotracheal tube. Study drugs (inj. dexamethasone 8 mg and inj. palonosetron 0.075 mg) were given i.v. just before induction of anesthesia. Anesthesia

was maintained with O₂ + N₂O mixture (33:66), halothane, and inj. vecuronium. Vitals were recorded at regular interval of 10 minutes throughout the procedure. Inj. diclofenac 75 mg i.v. was given to all the patients intraoperatively. Patients were extubated after giving inj. neostigmine 50 µg/kg and inj. glycopyrrolate 10 µg/kg. Occurrence of nausea, retching, and vomiting was recorded for 24 hours in the postoperative period. The rescue antiemetic used was i.v. metoclopramide (2 cc) for patients complaining of PONV. Patients were also asked for complaints such as headache, dizziness, diarrhea or constipation, allergy, and others, which were recorded, and appropriate treatment was done.

Statistical Analysis

Statistical analysis was performed using SPSS version 20 (SPSS Inc., Chicago, Illinois, USA). Categorical data were described as percentages and numerical data as means and standard deviations. Statistical tests applied for the analysis were one-way analysis of variance (ANOVA) and chi-square test. Precision of estimates was shown as 95% confidence limits. A p value of less than 0.05 was considered statistically significant. Mean and standard deviation were used to represent the average and typical spread of values. Data were expressed as frequency (%). Chi-square test was used for nonparametric data and ANOVA for parametric data. Post hoc Student's paired t -test was applied wherever indicated.

RESULTS

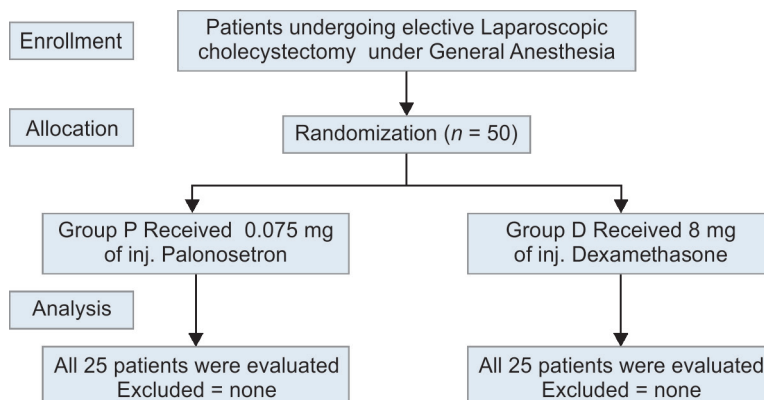
Fifty patients scheduled for laparoscopic cholecystectomy were randomized into two groups of 25 each, receiving either 8 mg dexamethasone or 0.075 mg palonosetron for prophylaxis of PONV (Flowchart 1).

The two groups were comparable in terms of mean age, body mass index (BMI), and gender distribution (Table 1). Intraoperative heart rate and blood pressure were also comparable in the two groups (Figs 1 and 2). The frequency of PONV (nausea, vomiting, or retching) in the two groups was comparable at 0, 1, and 2 hours. At 4, 8, and 12 hours, it was significantly less in patients receiving palonosetron than those receiving dexamethasone. At 24 hours, both groups were comparable (Table 2). No complications were observed.

DISCUSSION

PONV is the second most common complaint in the postoperative period after pain. A high frequency of PONV significantly interferes

Flowchart 1: Consort flow diagram



with smooth emergence from anesthesia and markedly increases patient discomfort in the postoperative period. The frequency of PONV is reported between 30% and 80% depending on the type of surgery and associated risk factors.^{1,8,9} CO₂ insufflation and peritoneal stretching are associated with PONV following laparoscopic cholecystectomy. Palonosetron is a newer congener of ondansetron with a longer half-life of around 40 hours and has not been associated with significant QT interval prolongation.⁶ Dexamethasone is a steroidal anti-inflammatory agent that has a central antiemetic action through the activation of glucocorticoid receptor in nuclei tractus solitarius in medulla. It decreases levels of 5-HT₃ in neural tissue and in the gut and is commonly used as an antiemetic agent in cancer chemotherapy and PONV. It has

low cost and prolonged biological half-life of 36–48 hours.⁷ The present study aimed to compare the effects of palonosetron and dexamethasone on the frequency of PONV in the patients undergoing laparoscopic cholecystectomy.

The frequency of PONV in the first 2 hours postoperative was 96–100% in both the groups and was comparable. At 4, 8, and 12 hours postoperative, respectively, 12, 4, and 1 patients receiving palonosetron had PONV compared to 21, 16, and 11 in those receiving dexamethasone. Thus, patients receiving palonosetron had significantly less PONV compared to those receiving dexamethasone. At 24 hours, only one patient in the dexamethasone group complained of PONV while none in the palonosetron group. This difference was statistically insignificant. Similarly, Chatterjee et al.¹⁰ reported a considerably high frequency of PONV in group D (dexamethasone—56.14%) than group P (palonosetron—27.2%) in the 24-hour postoperative period and concluded that 8 mg dexamethasone was less effective than 0.075 mg palonosetron in the prevention of PONV. The reported frequency of PONV was lower than our study, which could be explained by the use of ranitidine 150 mg as premedication and use of air instead of nitrous oxide.

Table 1: Demographic data

Parameters	Group D (n = 25)	Group P (n = 25)	p value
Age (years)	40.44 ± 10.35	41.88 ± 13.38	0.672
BMI (kg/m ²)	24.04 ± 0.79	24.08 ± 1.37	0.911
Gender (M/F)	17/8	20/5	0.333

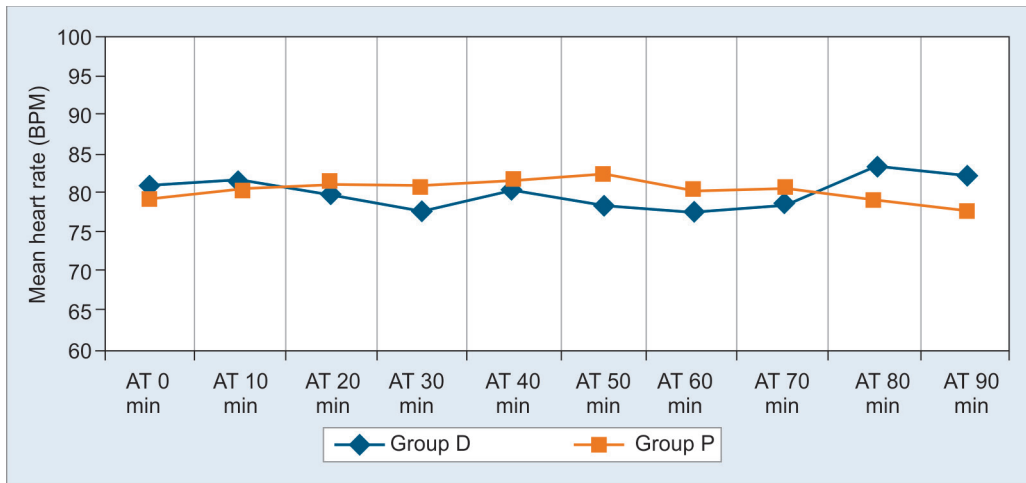


Fig. 1: Mean intraoperative heart rate in the study groups

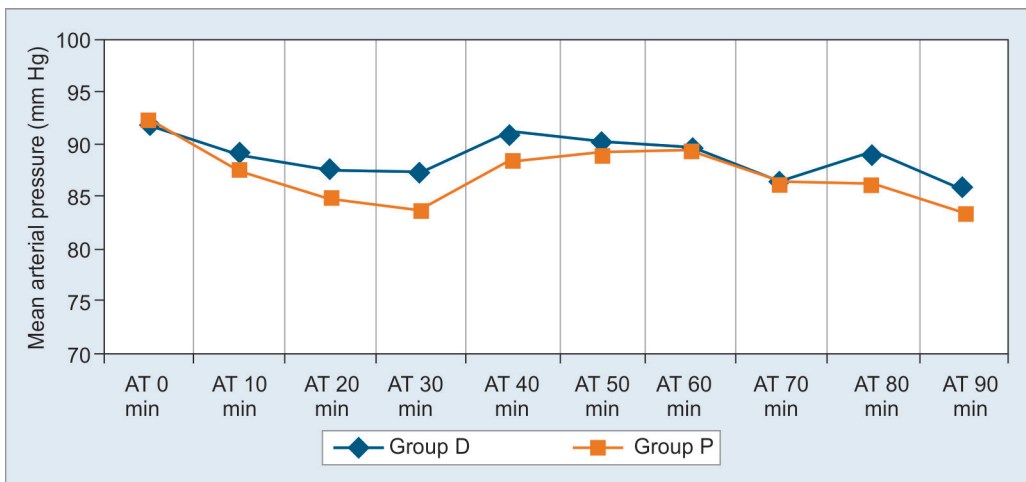


Fig. 2: Mean intraoperative mean arterial pressure in the study groups

Table 2: Frequency of PONV in the postoperative period

Parameter Time (hours)	Group D (n = 25)	Group P (n = 25)	p value
0 hour	25	25	—
1 hour	25	24	0.471
2 hours	24	25	0.471
4 hours	21	12	0.007*
8 hours	16	4	0.001*
12 hours	11	1	0.001*
24 hours	1	0	0.471

* = significant; $p < 0.05$ = significant

Tahir et al.¹¹ also reported a significantly higher frequency of nausea in group D (dexamethasone) as compared to group P (palonosetron), while the frequency of vomiting was comparable between the two groups from 0 to 6 hours postoperatively. From 6 to 48 hours, however, the frequency of nausea and vomiting was found comparable between the two groups, in contrast to our findings.

The mean age of participants was comparable between the study groups. Female gender is considered the strongest risk factor for PONV and it is three times more prevalent in adult females than in adult males.¹² Females were equally distributed among the study groups, and there was no statistical significance in the gender distribution. Some studies have suggested an increased risk of PONV in obese patients; however, the BMI has not been correlated with an increased risk of the development of PONV in recent studies.¹³ The BMI did not show any statistically significant difference between the two groups that could possibly affect the results. The mean arterial blood pressure was comparable among the groups. No episodes of hypertension or hypotension were observed. We did not observe any drug-related complications in the study participants.

CONCLUSION

We can conclude from the present study that in comparison to 8 mg dexamethasone, 0.075 mg palonosetron reduces the frequency of PONV after laparoscopic cholecystectomy.

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