e-ISSN: 0975-1556, p-ISSN:2820-2643

Available online on www.ijpcr.com

International Journal of Pharmaceutical and Clinical Research 2023; 15(9); 391-395

Original Research Article

Efficacy of Palonosetron and Dexamethasone for Prevention of Post-Operative Nausea and Vomiting in Patients Undergoing Laparoscopic Cholycystectomy

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Received: 25-06-2023 / Revised: 28-07-2023 / Accepted: 30-08-2023

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Conflict of interest: Nil

Abstract:

Background and Aim: PONV (postoperative nausea and vomiting) is a very uncomfortable and unpleasant symptom. Dexamethasone and palonosetron are antiemetic medications with few side effects. The current study was conducted with the goal of determining whether the combination of palonosetron and dexamethasone would be more effective as an antiemetic for PONV prophylaxis than either drug alone, and the study was designed to accept or reject that hypothesis.

Material and Methods: A double-blind, randomised interventional research was planned. The study involved 300 patients who met the inclusion criteria (age: 18-60 years, American Society of Anesthesiologists (ASA) physical status I and II, undergoing laparoscopic cholecystectomy under general anaesthetic). They were divided into three groups and assigned to one of three treatment regimens: (n = 100) in Group A Group B (n = 100) received Dexamethasone 8 mg plus Palonosetron 0.075 mg. Palonosetron 0.075 mg on its own OR Group C (n = 100) Dexamethasone 8 mg on its own. The primary outcome was the occurrence of PONV within 24 hours, while the secondary result was the number of rescue antiemetic medications required. To compare the means of the three groups, the one-way ANOVA test was performed.

Results: The overall occurrences of PONV in the study 24 h postoperatively were 20% in group A, 40% in group B, and 82% in group C (P 0.001). The dexamethasone group required more rescue antiemetic than the other two groups.

Conclusion: Palonosetron and palonosetron-dexamethasone combinations were more effective than dexamethasone alone in avoiding PONV in patients undergoing laparoscopic cholecystectomy.

Keywords: Dexamethasone, Nausea, Palonosetron, Vomiting.

Introduction

Post-operative nausea and vomiting (PONV) is a common consequence after anaesthesia that, despite recent breakthroughs in prophylaxis, can occur in up to 80% of patients depending on risk factors. [Though PONV is rarely connected with catastrophic squeals, it is an unpleasant experience associated with patient discomfort and discontent, delayed recovery room departure, a longer hospital stay, and higher health care expenses. [2-4] Repeated occurrences of PONV have been linked to more significant and unfavourable outcomes such as electrolyte imbalance, dehydration, and heightened pain perception, aspiration of gastric contents, oesophageal rupture, and suture dehiscence. [5,6] Although such catastrophic consequences are uncommon, procedures, particularly laparoscopic cholecystectomy, raise the risk of PONV by up to 50%. [7,8] The simplified risk score developed by Apfel Female gender, non-smoker status, a history of motion sickness, and usage of postoperative intravenous (IV) opioid all contribute 20% to the incidence of PONV. As a result, when all four risk factors are present, the incidence of PONV might reach 80%. [9] Female gender, non-smoker status, history of motion sickness, and usage of post-operative intravenous

(IV) opioid all contribute 20% to the incidence of PONV, according to Apfel's simplified risk score. As a result, when all four risk factors are present, the incidence of PONV might reach 80%. [9]

Various medicines, including anticholinergic, phenothiazine, antihistamines, butyrophenones, and steroids, have been used in the past to prevent PONV, but the majority of these have a short duration of action or are linked with side effects. Dexamethasone is extensively used to minimize PONV in all types of surgery. Its particular method of action is uncertain, but it has been proposed that it works by activating glucocorticoid receptors in the medulla, inhibiting central prostaglandin synthesis, or preventing endogenous opioid release. [10,11,12] 5-hydroxy trypamine receptor antagonist (5-HT3-RA) receptor antagonists, such as ondansetron, granisetron, and tropisetron, are considered very safe and effective antiemetic medicines. Palonosetron is a second-generation 5-HT3 receptor antagonist that prevents PONV better than granisetron 1 mg and ondansetron 4 mg. Dexamethasone has been shown to be both safe and effective in the prevention of PONV following various procedures. Although the majority of previous studies support the usage of dexamethasone with palonosetron, other investigations disagree. In this context, we hypothesised that combining palonosetron and dexamethasone as an antiemetic for PONV prophylaxis would be more effective than either drug alone, and this study was designed to confirm or refute that hypothesis.

Material and Methods

A double-blind, randomised interventional research was planned. After receiving informed and written agreement, 300 patients who met the inclusion criteria (age: 18-60 years, American Society of Anesthesiologists (ASA) physical status I and II, undergoing laparoscopic cholecystectomy under general anaesthetic) were entered in the study. Patients with a history of allergy or contraindication to any of the study drugs, pregnant and lactating mothers, patients with uncontrolled systemic diseases, a history of previous PONV and motion sickness, females in their premenstrual period, and patients weighing more than 75 kg were all excluded.

One independent investigator randomly assigned patients to one of three treatment regimens: (Group A) dexamethasone 8 mg with palonosetron 0.075 mg, (Group B) palonosetron 0.075 mg, and (Group C) dexamethasone 8 mg. All three medications were drawn into identical 5 mL syringes, diluted to 5 mL with normal saline, and labelled as "antiemetic." The research medicines were delivered gently over 30 seconds right before anaesthesia was induced. The group allocation was unknown to the patients, anesthesiologists participating in intra-operative care, and the investigator collecting data in the post-operative ward.

The patient was premedicated with injections of Glycopyrrolate 0.01 mg/kg, midazolam 0.03 mg/kg, fentanyl 2mcg/kg, and thiopentone 2-5 mg/kg. Atracurium 0.5mg/kg injection aided endotracheal intubation. Mechanical ventilation was controlled, and anaesthetic gases (sevoflurane in 50% O2 and nitrous oxide) were administered. Intra-operative monitoring included a 5-lead ECG, SpO2, EtCO2, and non-invasive blood pressure. Extubation was performed at the end of surgery after restoring any residual muscle paralysis with injections of neostigmine 0.05 mg/kg and glycopyrrolate 4 mcg/kg. Patients were sent to the postanaesthesia care unit (PACU) following extubation. Diclofenac 1 mg/kg injection was administered as postoperative analgesia and was repeated every 8 hours.

In the PACU, all patients were monitored. The primary outcome was the occurrence of nausea and vomiting within 24 hours. The number of rescue antiemetic doses required was a secondary result. As a rescue antiemetic, injection metoclopramide 10 mg IV was administered. The unpleasant sensation linked with the consciousness of the desire to vomit was characterised as nausea, and vomiting was defined as the forceful evacuation of gastric contents from the mouth. Any episode of nausea, vomiting, retching, and/or usage of a rescue antiemetic was considered a failure of PONV prophylaxis. The occurrence of any PONV and the number of rescue antiemetic required were assessed at 0, 1, 2, 6, 12, and 24 hours postoperatively. PONV was calculated as follows: 1 = no nausea and vomiting; 2 = nausea but no vomiting; 3 = nausea and vomiting.

Statistical investigation

The collected data was assembled and input into a spread sheet programme (Microsoft Excel 2007) before being exported to the data editor page of SPSS version 15 (SPSS Inc., Chicago, Illinois, USA). The confidence level and level of significance for all tests were set at 95% and 5%, respectively.

Results

There were no statistically significant variations in age, gender, or ASA physical status between the groups.(Table 1) Immediately after transferring the patient to the post-operative area, the incidence of PONV was 6%, 10%, and 40% in the A, B, and C groups, respectively (P 0.001). After 1 hour, 16% of the A group, 16% of the B group, and 26% of the C group reported PONV (P = 0.343). Nobody in the A group experienced PONV at 2 hours

postoperatively, whereas 6% in the P group and 12% in the C group did (P = 0.03). At 6t h, no patient in the A group, 8% in the P group, and 8% in the C group reported PONV (P = 0.48) (Table 2). In our investigation, no patient reported nausea or vomiting after 6 hours and up to 24 hours postoperatively. In our study, the overall occurrences of PONV (primary outcome) were 20% in the A group, 40% in the B group, and 82% in the C group 24 hours after surgery (P 0.001). C > B > A groups required considerably more rescue antiemetic.

Table 1: Demographic profile of study groups

Variable	Group A (N=100)	Group B (N=100)	Group C (N=100)	P value
Age (Years) Mean±SD	40.12±10.15	39.22±11.03	42.94±13.47	0.32
Gender (Male/Female)	28/72	25/75	30/70	0.10
ASA physical status I II	35 (70%) 15 (30)	37 (74%) 13 (26)	35 (70%) 15 (30)	0.45

P<0.05 considered as significant SD – Standard deviation; ASA – American Society of Anesthesiologists.

Table 2: Incidence of postoperative nausea and vomiting in postoperative period in all groups

PONV		A (%)		B (%)		C (%)		P value
0 h	Yes	6	6	10	10	20	20	0.05*
	no	94	94	90	90	80	80	
1 h	Yes	16	16	16	16	26	26	0.1
	no	84	84	84	84	74	74	
2 h	Yes	0	0	6	6	14	14	0.03*
	no	100	100	94	94	86	86	
6 h	Yes	0	0	8	8	7	7	0.48
	no	100	100	92	92	93	93	
12 h	Yes	0	0	0	0	0	0	-
	no	100	100	100	100	100	100	
24 h	Yes	0	0	0	0	0	0	-
	no	100	100	100	100	100	100	

P < 0.05 considered as significant.

Discussion

PONV is one of the most feared side effects of surgery under general anaesthetic. In our investigation, a single dosage of palonosetron was found to be as effective as dexamethasone in avoiding PONV in adult female patients following laparoscopic abdominal operations. Female gender, a history of motion sickness or PONV, being a nonsmoker, and using perioperative painkillers are all risk factors for PONV. If none, one, two, three, or four of these risk factors are present, the incidence of PONV is reported to be 10, 20, 39, 61, and 79%. [1]

Palonosetron is a highly effective 5-HT3 antagonist with a lower adverse effect profile than other medications previously used to prevent and treat PONV. Dexamethasone is believed to be an efficient antiemetic with central antiemetic activity via activation of glucocorticoid receptors in the medulla's bilateral nucleus tractus solitarii.

Dexamethasone was the least effective as a single medicine in our trial, but it was more beneficial when combined with palonosetron than when used alone.

The overall incidence of PONV in the first 24 hours was highest in the dexamethasone alone group, while palonosetron alone and in combination groups had significantly lower incidences. The incidence of PONV did not differ statistically between the Palonosetron and combination groups. Palonosetron and its combination with dexamethasone are both efficacious; however the combination is not superior to palonosetron alone. Dexamethasone in combination with palonosetron, as opposed to dexamethasone alone, significantly reduced the incidence of PONV at 12-24 hours post-operatively, according to Emad E. Mansour et al. [13]. In a trial of Korean women, the combination of palonosetron and dexamethasone was more effective than dexamethasone alone in decreasing PONV. However, as compared to palonosetron alone, the combination did not provide any extra benefits in avoiding PONV following thyroidectomy. [14] Palonosetron monotherapy was proven to be as effective as its combination with dexamethasone in prior investigations of outpatient laparoscopy. [15,16] This shows that palonosetron is efficacious enough on its own and does not need to be combined in low to moderate risk patients.

For patients with PONV, injection metoclopramide (10 mg) was utilised as a rescue antiemetic. Despite the fact that metoclopramide is a mild antiemetic in comparison to 5-HT3 blockers, we picked it since it is widely available and utilised as an antiemetic medicine in our institute with a reasonable adverse effect profile. Its mode of action (D2 receptor

blockage) is likewise distinct from the medications under consideration.

Patients in the dexamethasone group required more rescue antiemetic than the other two groups. Dexamethasone is a corticosteroid having potent anti-inflammatory and antiemetic properties. In a variety of clinical contexts, it has been found to be an effective antiemetic. [17,18]

Dexamethasone has been shown to be as effective as or more effective than 5HT-3 receptor antagonists such as granisetron in preventing PONV during cancer chemotherapy. [16] Palonosetron injection is a new, potent and long acting 5- HT3 receptor antagonist. Palonosetron has also been reported to be superior to other 5-HT3 antagonist like ondansetron, and granisetron in previous studies comparing them for PONV prophylaxis. [17]

We also studied the trend of incidence of PONV overtime for first 24 h and we found that no patient complained of PONV in three study groups after 6 h. This result is variable from other studies, which showed a variable incidence of PONV continuing in the first 24 h and beyond. [19,20] Dexamethasone is known to cause side effect such as increased incidence and severity of infection, adrenal suppression and delayed healing in surgical patients. [21] There are few limitations in our study. Pre-operative medications for chronic co-morbidity could not be controlled.

Post-operative nil per oral status and diet were not identical in all patients. As this was a single centre trial. If the study was conducted multicentrically, the generalisability would have increased as the study drugs could have been tested in geographically distinct populations.

Conclusion

Palonosetron and palonosetron-dexamethasone combinations were more effective than dexamethasone alone in avoiding PONV in patients undergoing laparoscopic cholecystectomy.

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