



A Study to Compare the Efficacy of Ondansetron and Palonosetron for Prevention of Post Operative Nausea and Vomiting in Patients Undergoing Laparoscopic Cholecystectomy

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ABSTRACT

BACKGROUND: This study was undertaken to compare the efficacy and safety of palonosetron and ondansetron for prevention of postoperative nausea and vomiting .

Materials and Methods: A total of 100 patients ASA grade I & II between 18-65 years of age , were randomly assigned into one of the two groups, containing 50 patients each.. Group palonosetron received palonosetron .075mg i.v. and Group ondansetron received ondansetron 8mg i.v. The incidence of nausea, retching and vomiting, VAS score for severity of nausea, requirement of rescue antiemetics and adverse effects were evaluated during the first 24hr following end of surgery.

RESULTS: The incidence of nausea was significantly lower in the palonosetron group (12%) compared to ondansetron group (30%). Patients requiring rescue antiemetics was significantly lower in the palonosetron group (18%) compared to ondansetron (40%).The PONV score was also significantly lower in the group palanosetron (28%) as compared to ondansetron (52%).

Conclusion: The incidence of nausea was significantly lower in the palonosetron group, a lesser need for rescue antiemetic postoperatively and more patients in palonosetron group had a complete response.

KEYWORDS

Palonosetron, Ondansetron, PONV, Laparoscopic Cholecystectomy

Introduction

Besides postoperative pain, postoperative nausea and vomiting (PONV) is the most frequent and most unpleasant adverse outcome of surgery and general anaesthesia.^[1] The incidence of PONV is estimated at 25% to 30% in all patients and as high as 80% in patients with multiple high-risk factors.^[2,3] PONV is distressing and potentially detrimental to a patient's recovery as it can result in wound dehiscence, bleeding, aspiration of gastric contents, electrolyte imbalances, and delayed hospital discharge.^[4] Laparoscopic cholecystectomy has rapidly emerged as an alternative to open cholecystectomy and is a routinely performed procedure for symptomatic cholelithiasis.^[5] The incidence of PONV following laparoscopic cholecystectomy is as high as 46 to 72 %.^[6] The traditional antiemetics, including anticholinergics and dopamine receptor antagonists, have been studied with regard to their efficacy for the prevention and treatment of PONV , however these agents have been reported to have adverse effects such as excessive sedation, hypotension, dysphoria, hallucinations, and extrapyramidal signs.^[2,7] The newest class used for prevention and treatment of PONV are 5-HT₃ receptor antagonists and are now a first line option because of effectiveness, more safety and favourable side-effects profile as they lack the sedative, dysphoric and extra-pyramidal side effects of other drugs.^[8,9,10,11] Ondansetron was the first 5-HT₃ receptor antagonist, it has a relatively short half life of 3-5hours, and its antiemetic efficacy has been well established in chemotherapy-induced emesis and the prevention and treatment of PONV.^[12-16] Second generation 5HT₃ antagonist, palonosetron was initially approved for prophylaxis of nausea and vomiting in cancer patients, as it improves the prevention of chemotherapy induced nausea and vomiting and proved superior to ondansetron in these patients, because of its unique chemical structure, greater binding affinity with additional allosteric site binding property and a substantially longer half-life of almost 40 hours made palon-

osetron suitable for its use in prevention of PONV.^[12,17,18,19] This study was undertaken to compare the efficacy and safety of palonosetron and ondansetron for prevention of postoperative nausea and vomiting in patients undergoing laparoscopic cholecystectomy under general anaesthesia.

Material and method

The study was conducted at National Institute Of Medical Sciences and Research medical college and hospital, jaipur after ethical committee approval and patient's informed written consent. 100 ASA grade I and II adult patients aged 18 to 65 yrs undergoing elective laparoscopic cholecystectomy were randomly allocated to receive one of the two study drugs: Palonosetron group, Palonosetron 0.075 mg i.v.; ondansetron group, ondansetron 8 mg i.v. 5 minutes just before the induction of general anaesthesia. Patients with ASA grade III, IV, V, taking opioid on a regular, daily basis for more than 3 consecutive days before surgery, persistent or recurrent nausea/vomiting due to other etiologies, had known hypersensitivity or contraindication to palonosetron, ondansetron or any other 5-HT₃ receptor antagonist were excluded from the study.

All patients were premedicated with midazolam (0.02mg/kg), glycopyrolate (0.004mg/kg) and fentanyl 2–3 µg/kg. Induction was done with propofol 2 mg/kg. Succinylcholine 2mg/kg was administered to facilitate tracheal intubation. Anaesthesia was maintained with isoflurane (1–2.5%) and nitrous oxide (66%) in oxygen. Muscle relaxation was maintained with boluses of injection vecuronium bromide with intermittent positive pressure ventilation. At the end of surgery, residual neuromuscular block was reversed with neostigmine (0.05mg/kg) and glycopyrrolate (0.008mg/kg). For post-operative analgesia, injection diclofenac sodium 1mg/kg intramuscularly was administered before shifting.

The incidence of PONV, severity of nausea, and the need for rescue antiemetics were evaluated for 24 h after surgery at intervals: 0–8h, 8-24h. Nausea defined as a subjectively unpleasant sensation associated with awareness of the urge to vomit, where as an episode of vomiting was defined as either vomiting (expulsion of stomach contents) or retching (an involuntary attempt to vomit but not productive of stomach contents). The intensity of nausea episode was assessed using a visual analogue scale (VAS) (0, no nausea; 10, worse nausea) [20] and retching and vomiting assessed by simply questioning for yes or no. No retching or vomiting scored 0 and yes scored 1. Rescue medication for PONV (metoclopramide 10 mg as an initial rescue drug) was administered upon patient request or complaint of established nausea (VAS score >5) or vomiting. No use of rescue medication scored as 0 and if used scored as 1. PONV score means the total no. of the patients who suffered either from nausea or emesis (vomiting/retching) or if needed rescue medication. A complete response was defined as the absence of PONV and no use of rescue antiemetics. Adverse events were evaluated and recorded by the investigator during the entire observation period.

The student's t-test was used to compare intergroup differences and the Chi-square tests were used for categorical variables. The P-value < 0.05 was regarded as statistically significant.

Results

There were no significant differences between the two groups with respect to age, sex, weight, duration of surgery or anaesthesia. [Table 1] The incidence of nausea was significantly lower in the palonosetron group (12%) compared to ondansetron group (30%) (P<0.05). The proportion of patients requiring rescue antiemetics was significantly lower in the palonosetron group (18%) compared to ondansetron group (40%) (P<0.05). The PONV score was also significantly lower in the group which had received palonosetron (28%) as compared to patients who had received ondansetron (52%). The incidence of complete response for palonosetron group (72%) and ondansetron group (48%) statistically significant (P<0.05). There were no significant differences with regard to the severity of nausea (VAS score) incidence of vomiting/retching in palonosetron group (18%) and ondansetron group (34%) (P >0.05). [Table 2] Furthermore, there were no statistically significant differences in the incidence of adverse events among the two groups. [Table 3]

Discussion

Despite continuing advances in anaesthetic technique and surgical skills PONV is the most frequent and most unpleasant adverse outcome of surgery and general anesthesia.[1] The incidence of PONV following laproscopic cholecystectomy is as high as 46 to 72 %.[6] All patients in our study underwent laparoscopic cholecystectomy, duration of anaesthesia, surgery and anaesthetic drugs were similar in both the groups. Therefore, we believe that the differences in the incidence of PONV were attributed to the study drugs.

Various drug regimes and antiemetic interventions have been tried for prevention of PONV, but a satisfying therapeutic coverage in patients has not yet been achieved by the current array of agents including older 5-HT3 antagonists which do not seem to offer adequately long protection.

Palonosetron has already been proven effective and safe in prevention of Chemotherapy induced nausea and vomiting. [12, 17, 18, 19] Therefore, we decided to conduct a study to evaluate and compare the efficacy of palonosetron which is a newer 5-HT3 antagonist against ondansetron.

The study dose of i.v. Ondansetron was 8mg and that of i.v. Palonosetron was .075mg, which was as per the recommendations of Tramer and colleagues and Candiotti et al. [19, 21]

The need for rescue antiemetic in our study was significantly higher in the Ondansetron group (40%) as compared to pa-

lonosetron (18%), which is due to the weaning of antiemetic effect of i.v. Ondansetron which lasts for 4-5 h. In our study, the overall incidence of PONV score was found to be (28%) in group palonosetron and (52%) in group ondansetron, due to difference in t½. [22]

The comparative efficacy of palonosetron versus ondansetron has not been much demonstrated previously in laparoscopic cholecystectomy and mainly placebo has been used for comparison in clinical trials.[18, 19, 23] However recently few studies have come up which have compared palonosetron with ondansetron and our results are also similar to them. Palonosetron was found to be more effective than ondansetron for high risk patients receiving fentanyl-based patient controlled analgesia after thyroidectomy in the 2-24 h period following surgery [24]. A single dose of palonosetron (250 mcg) was found to be a superior antiemetic to ondansetron (8 mg) in complete prevention of PONV after middle ear surgery during the first 24h postoperative period. [25] In a randomized controlled trial in day care surgery, single pre-induction i.v. dose of palonosetron (75 mcg) proved to be superior to ondansetron(8 mg) in terms of the number of subjects experiencing PONV episodes and the dose of rescue antiemetic required. [22] The incidence of PONV has been found to be significantly lower with palonosetron than with ondansetron in gynecological laproscopic surgeries, although there were no significant differences in VAS scores for nausea. [26]

Conclusion

The incidence of nausea (not vomiting) was significantly lower in the palonosetron group, a lesser need for rescue antiemetic postoperatively and more patients in palonosetron group had a complete response.

Table 1. Patient characteristics Data are Mean+/-SD, number (%)

	Palonosetron (n=50)	Ondansetron (n=50)
Age	41.60+/-11.19	42.78+/-10.96
Sex	M:8(16), F:42(84)	M:10(20), F:40(80)
Weight	68.2+/-5.4	66.8+/-4.8
Surgery (min)	60.8+/-8.2	62.4+/-7.8
Anaesthesia (min)	87.4+/-5.8	86.8+/-6.4

Table 2. Incidences of nausea, Vomiting, PONV score, VAS score, Rescue antiemetics, Complete response.

	Palonosetron (n=50)	Ondansetron (n=50)
0-8 hrs	Mean+/- SD, number (%)	Mean+/- SD, number (%)
Nausea	3(6)	8(16)
Vomiting/retching	2(4)	3(6)
Ponv score	5(10)	10(20)
Vas score	3.75+/-0.96	4.11+/-1.36
8-24 hrs	Mean+/- SD, number (%)	Mean+/- SD, number (%)
Nausea	4(8)	6(12)
Vomiting/retching	3(6)	5(10)
Ponv score	6(12)	8(16)
Vas score	4.25+/-1.50	3.83+/-0.98
0-24 hrs	Mean+/- SD, number (%)	Mean+/- SD, number (%)
Nausea	6(12)	15(30)
Vomiting/retching	9(18)	17(34)
Ponv score	14(28)	26(52)
Vas score	5.58+/-2.27	5.39+/-2.23
Rescue antiemetics	9(18)	20(40)
Complete response	36(72)	24(48)

Table 3. Incidences of adverse event.

	Palonosetron (n=50)	Ondansetron (n=50)
Side effects		
Headache	2(4)	3(6)
dizziness	1(2)	2(4)

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