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Original Research Article

A Randomized, Double-Blind Trial of Palonosetron Compared with Ondansetron in Preventing Postoperative Nausea and Vomiting after Gynaecological Laparoscopic Surgery

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Abstract

This randomised, double-blind trial compared the effectiveness of ondansetron and palonosetron in reducing postoperative nausea and vomiting (PONV) in patients following gynaecological laparoscopic surgery. Palonosetron is a novel, selective 5-hydroxytryptamine type 3 [5-HT_3] receptor antagonists. Right before general anaesthesia was induced, patients were given either palonosetron 0.075 mg (n = 45) or ondansetron 8 mg (n = 45), intravenously. Immediately following the conclusion of surgery and for the next 24 hours, the occurrence of nausea and vomiting as well as the degree of that nausea as measured by a visual analogue scale were observed. When compared to the ondansetron group, the incidence of PONV was considerably lower in the palonosetron group (42.2% vs. 66.7%, respectively). The visual analogue scale for nausea showed no statistically significant changes. In conclusion, palonosetron 0.075 mg prevented PONV better than ondansetron 8 mg.

Keywords: palonosetron, ondansetron, 5-HT_3 receptor antagonist, postoperative, nausea and vomiting (ponv), gynaecological laparoscopic surgery

Introduction

The most frequent side effect of anaesthesia and surgery is postoperative nausea and vomiting (PONV) [1] which can have a negative impact on patients and cause unexpected hospital admissions, delayed recovery, and missed employment opportunities. More severe postoperative consequences such wound dehiscence and surgical site haemorrhage are less frequently linked to PONV [2,3]. In high-risk patients, the incidence of PONV might exceed 80%, highlighting the significance of anaesthetists' preventative and control measures [4].

5-hydroxytryptamine-3 (5-HT3) receptor antagonists are frequently prescribed drugs for PONV prophylaxis because to their similar efficacy to droperidol or

dexamethasone and their favourable side-effect profile [2]

Palonosetron is a brand-new, highly effective 5-HT_3 receptor antagonist that is selective, has a high affinity for the receptor, and has a protracted half-life after elimination [5,6] A single 0.075 mg intravenous (i.v.) dose of palonosetron significantly reduced emetic episodes, nausea severity, and rescue medication use in patients undergoing abdominal or gynaecological laparoscopic surgery during the first 24 hours following anaesthesia, according to a study evaluating the effectiveness and safety of the drug in preventing PONV [7] Despite the fact that no study has compared the relative effectiveness of palonosetron and ondansetron in avoiding PONV, it has been reported that palonosetron is just as effective as ondansetron in preventing chemotherapy-induced nausea and vomiting after highly emetogenic chemotherapy [8].

In order to examine the effectiveness of palonosetron and ondansetron in avoiding PONV in patients undergoing laparoscopic gynaecological surgery, the current randomised, double-blind trial was created.

Material and methods

The study included patients who were scheduled to have elective laparoscopic gynaecological surgery lasting longer than one hour at Department of Anaesthesia and Critical Care, VMMC & Safdarjung Hospital, New Delhi, between January 2022 and June 2022 and who were ≥21 years old and had physical status 1 or 2 [9] according to the American Society of Anesthesiologists.

There were at least two risk indicators for PONV in every patient who was included because they were all female and used opioids to manage post-operative pain. Patients who had used antiemetics, steroids, or psychoactive drugs within 24 hours of the study's start were disqualified from participation. All participants gave written informed consent before being enrolled, and those who had had vomiting or retching in the 24 hours prior to surgery, cancer chemotherapy within 4 weeks prior to study enrollment, or emetogenic radiation within 8 weeks prior to study entry, were excluded.

Palonosetron 0.075 mg or ondansetron 8 mg was given to patients at random as an intravenous injection. The medications were made as directed by the makers and placed in numbered, sealed envelopes with numbers provided using computer-generated random numbers by trained nurses who did not take part in the study. Preanaesthetic medicine was not given to any patients.

Prior to inducing anaesthesia, individuals in the palonosetron group received a single i.v. dosage of palonosetron 0.075 mg with the addition of saline solution to make the total volume 4 ml. Ondansetron 8 mg was administered intravenously in a single dosage as a 4 ml bolus to participants in the ondansetron group just before to the onset of anaesthesia.

All patients received standard anaesthesia protocols. Rocuronium 0.6 mg/kg was used to assist tracheal intubation while propofol 2 mg/kg was used to induce anaesthesia. Sevoflurane and 50% nitrous oxide in oxygen were used to maintain anaesthesia. Patients were given pyridostigmine (0.2 mg/kg) and glycopyrrolate (0.008 mg/kg) after surgery to reverse the neuromuscular blockade. A patient-controlled anaesthesia device was utilised to administer a fentanyl 4 μg bolus with a background infusion of 16 μg/h, with a 15 min lockout time, for the purpose of controlling postoperative pain.

Immediately following the conclusion of surgery, as well as at 0–2 h, 2–6 h, and 6–24 h afterward, rescue antiemetic medicine use was observed, together with the incidence of nausea and vomiting and the severity of that nausea as measured by a visual analogue

scale (VAS; 0, no nausea; 10, severe sickness). An episode of vomiting was described as the forced expulsion of gastric contents from the mouth, whereas nausea was defined as a subjectively unpleasant sensation linked with awareness of the want to vomit (laboured, spasmodic, rhythmic contractions of the respiratory muscles without expulsion of gastric contents). 1 When two bouts of PONV occurred or when the patient sought therapy and the VAS was greater than 5, metoclopramide (10 mg i.v.) was allowed as a rescue antiemetic.

Ondansetron 4 mg intravenously was allowed if metoclopramide treatment proved ineffective. Absence of PONV and non-use of rescue antiemetics were considered signs of a full response.

Any negative symptoms, such as headaches, lightheadedness, constipation, and myalgia, were noted in detail. A three-point scale (satisfied, neutral, and unhappy) was also used to gauge patient satisfaction 24 hours after surgery.

The frequency of nausea and vomiting in the first 24 hours following anaesthesia served as the study's major outcome indicator. Severity of nausea, the necessity for rescue medication, patient satisfaction, and the frequency of negative effects were secondary outcome variables.

In order to demonstrate a 30% difference in the incidence of PONV, it was anticipated that a minimum of 42 patients per group would be needed, with an allowance for a -error of 5% and a -error of 20% [7-10].

The SPSS® statistical package for Windows®, version 17.0 (SPSS Inc., Chicago, IL, USA), was used for all statistical analyses.

For categorical variables, the Student's t-test or Fisher's exact test was employed to compare intergroup differences. A P-value of <0.05 or lower was considered statistically significant after the P-values were corrected using the Bonferroni technique.

Results

All 90 patients who were enrolled in the trial finished it. Regarding patient characteristics, risk factors for PONV, or information regarding the operation, there were no statistically significant differences between the groups receiving palonosetron and ondansetron treatment (Table 1).

Table 1: Baseline demographic data and clinical characteristics for patients undergoing laparoscopic gynaecological surgery who received ondansetron 8 mg or palonosetron 0.075 mg, intravenously, before anaesthesia

	Ondansetron group (n=45)	Palonosetron group (n=45)
Age (in years)	42.8±7.3	42.4±10.0
Weight (in kg)	55.3±7.3	56.9±7.8
Height (in cm)	157.6±5.5	158.3±6.2
ASA Physical status		
1	37(82.2)	40(88.9)
2	8(17.8)	5(11.1)
Risk factors		
PONV history and/or motion sickness	19(42.2)	20(44.4)
Non-smoker	43(95.6)	39(86.7)
Type of surgery		
Laparoscopic ovarian cystectomy	18(40.0)	17(37.8)

Laparoscopic hysterectomy	27(60.0)	28(62.2)
Duration of surgery (min)	108.6±45.2	103.3±35.3
Duration of anaesthesia (min)	137.1±48.2	130.4±35.2

Data presented as mean ± SD or *n* (%) of patients.

No statistically significant between-group differences ($P > 0.05$); Student's *t*-test and Fisher's exact test. ASA PS, American Society of Anesthesiologists; PONV, postoperative nausea and vomiting. Over the course of the entire 0 - 24 h time period, the incidence of PONV and nausea (but not vomiting) was significantly lower in the palonosetron group than in the ondansetron group (P <0.05, Table 2).

Table 2: Incidence of post-operative nausea and vomiting (PONV), need for rescue antiemetics, and severity of PONV in patients undergoing laparoscopic gynaecological surgery who received ondansetron 8 mg or palonosetron 0.075 mg, intravenously, before anaesthesia

	Ondansetron group (n=45)	**Palonosetron group (n=45)**
0 – 2 hours		
• Nausea	12(26.7)	4(8.9)
• Vomiting	0(0)	3(6.7)
• Overall PONV	12(26.7)	7(15.6)
• VAS	1.5±2.7	1.0±2.8
2 – 6 hours		
• Nausea	10(22.2)	5(11.1)
• Vomiting	3(6.7)	2(4.4)
• Overall PONV	13(28.9)	7(15.6)
• VAS	2.2±4.3	2.1±3.1
6 – 24 hours		
• Nausea	15(33.3)	9(20.0)
• Vomiting	6(13.3)	4(8.9)
• Overall PONV	21(46.7)	13(28.9)
• VAS	3.4±4.9	3.4±4.5
0 – 24 hours		
• Nausea	27(60.0)	15(33.3)*
• Vomiting	7(15.6)	8(17.8)
• Overall PONV	30(66.7)	19(42.2)*
• VAS	4.5±4.9	4.1±4.9
Rescue antiemetics	7(15.6)	8(17.8)

Data presented as mean ± SD or *n* (%) of patients.

*$P < 0.05$ for the palonosetron group compared with ondansetron group; Student's *t*-test and Fisher's exact test. VAS, visual analogue scale for severity of nausea: 0, no nausea; 10, worst nausea.

In comparison to the ondansetron group, more patients in the palonosetron group experienced a full response (no PONV and no rescue antiemetic); this difference was statistically significant for the time period of 0 to 24 hours (P <0.05). There was no discernible difference between the two

groups in terms of the severity of nausea (VAS), the requirement for rescue antiemetics, the frequency of negative side effects, or patient satisfaction ratings (Table 3).

Table 3: Incidence of adverse events and satisfaction in patients undergoing laparoscopic gynaecological surgery who received ondansetron 8 mg or palonosetron 0.075 mg, intravenously, before anaesthesia

	Ondansetron group (n=45)	Palonosetron group (n=45)
Adverse event		
• Headache	4(8.9)	3(6.7)
• Dizziness	5(11.1)	5(11.1)
• Constipation	2(4.4)	3(6.7)
• Myalgia	0(0)	1(2.2)
Patient satisfaction		
• Satisfied	21(46.7)	30(66.7)
• Neutral	17(37.8)	9(20.0)
• Dissatisfied	7(15.6)	6(13.3)

Discussion

Despite the widespread use of preventative antiemetics, such as 5-HT_3 receptor antagonists, many individuals still have PONV [11]. The 5-HT_3 receptor antagonist ondansetron was the first to enter the market, and it has been used often to manage PONV [12]. Second-generation 5-HT_3 antagonist palonosetron stands out from previous 5-HT_3 antagonists thanks to its distinct structural, pharmacological, and therapeutic characteristics [2] Palonosetron and ondansetron for PONV are being compared for the first time in this study.

In comparison to placebo, 0.075 mg of palonosetron considerably decreased PONV in the first 24 hours following anaesthesia, according to Kovac *et al* [7]. The effectiveness of 4 mg versus 8 mg ondansetron for the prevention of PONV following laparoscopic cholecystectomy was also examined by Paventi *et al* [13] who found that 8 mg was more effective than 4 mg. 0.075 mg of palonosetron and 8 mg of ondansetron were selected as the medication doses employed in the current trial because they were found to be the most effective for the prophylaxis of PONV in these earlier investigations. Palonosetron 0.25 mg has been demonstrated by certain researchers to be as secure and successful as ondansetron 32 mg in avoiding chemotherapy-related nausea and vomiting (CINV) [14].

The pathophysiology of PONV is more complex and has been hypothesised to have a multifactorial origin, in contrast to the aetiology of CINV, which is principally related to a significant release of serotonin from the enterochromaffin cells in the small intestine in response to chemotherapeutic drugs [15].

The prevalence of PONV may be influenced by a number of variables, including age, gender, smoking status, postoperative opioid use, kind and duration of surgery, anaesthesia, ambulation, and gender (female gender and younger age in adulthood enhance the risk of PONV) [16,17]. In the current investigation, these variables were evenly distributed between the two therapy groups. In the current trial, palonosetron 0.075 mg was more efficient than ondansetron 8 mg for lowering PONV. This may be due to palonosetron's high receptor affinity for 5-HT_3, poor affinity for other

receptors like 5-HT_{1A}, 5-HT_{1D}, 5-HT_{2A}, and 5-HT_{2C}, and palonosetron's prolonged duration of action [5-18].

The incidence of vomiting was somewhat higher in the palonosetron group than in the ondansetron group, albeit this difference was not statistically significant. This may be because ondansetron has a stronger antiemetic (rather than antinausea) impact [19].

In terms of preventing vomiting, ondansetron is vastly superior to metoclopramide and droperidol [20] however, it is unknown if this antiemetic action is more potent than that of palonosetron. Serotonin 5-HT_3, dopamine D_2, histamine H_2, α_2-adrenergic, muscarinic cholinergic, neurokinin1, and GABA are just a few of the receptor types that play a part in the start and coordination of the vomiting reflex in PONV patients [15-20].

Palonosetron may be less effective than ondansetron at reducing the frequency of vomiting because ondansetron has a weaker affinity for binding to 5-HT_{1B}, 5-HT_{1C}, α–adrenergic, and μ-opioid receptors [21] though more research is required to make sure of this. In the current investigation, there were no differences in the degree of nausea or the requirement for further rescue antiemetics between the two groups.

The current investigation demonstrated that individuals with moderate or high PONV risk—those with at least two PONV risk factors—remained at high risk for PONV even after receiving preventive ondansetron or palonosetron therapy.

Thus, multimodal prophylaxis should be given to patients who are at moderate or high risk of PONV [4,22-24]. Improved efficacy, a longer duration of the antiemetic effect, the ability to combine drugs with greater antinausea versus greater antiemetic effects, and the potential to use lower doses of individual drugs compared to monotherapies are some potential benefits of combination therapy using drugs that act on different pathways in the emetic response [25].

Granisetron 3 mg and droperidol 1.25 mg were found to work better together than either antiemetic alone in a previous research to prevent PONV [26]. In a different trial, PONV prevention in patients undergoing laparoscopic cholecystectomy was found to be more successful with ondansetron 4 mg and dexamethasone 8 mg than with ondansetron alone [27]. These findings imply that the combination of palonosetron and either droperidol or dexamethasone may be efficient in preventing PONV.

The control of nausea and vomiting during the second and third postoperative days is improved by palonosetron 0.075 mg, administered intravenously [28].

In contrast to ondansetron, which has a half-life of 3 to 5 hours, palonosetron has a long half-life of about 40 hours [29]. This could help to offset the more expensive price of this newly created medication. To assess the ability of palonosetron and ondansetron to minimise PONV 24–72 hours postoperatively, more studies are required [30].

With the majority of adverse effects (such as headache, constipation, and dizziness) being mild and temporary, 5-HT_3 antagonists have an admirable safety record [31].

Palonosetron has a comparable safety profile to other 5-HT_3 antagonists [32] and in the current investigation, there was no difference in the occurrence of negative effects between the two groups.

The effectiveness of palonosetron and ondansetron was compared based on known optimal doses, without knowledge of equipotent doses; the power analysis was conducted using patients who did not

undergo identical types of surgery to estimate the expected incidence of PONV; and finally, the baseline incidence of PONV was not assessed by including a placebo group because it would be unethical to withhold prophy.

Conclusion

In conclusion, palonosetron 0.075 mg i.v. produced a lower incidence of PONV compared with ondansetron 8 mg i.v. in patients undergoing laparoscopic gynaecological surgery.

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