

“A COMPARISON OF ONDANSETRON AND PALONOSETRON FOR PREVENTION OF POST-OPERATIVE NAUSEA AND VOMITING IN PATIENTS UNDERGOING ELECTIVE ABDOMINAL SURGERIES UNDER GENERAL ANAESTHESIA” A RANDOMIZED DOUBLE BLIND STUDY

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ABSTRACT

Background: Post-operative nausea and vomiting (PONV) is commonly seen in female patients undergoing abdominal surgeries under general anaesthesia. In this randomized double blind prospective study, efficacy of ondansetron and palonosetron for prevention of PONV following abdominal surgeries under general anaesthesia was compared.

Methods: 60 female patients undergoing elective abdominal surgery were randomly allocated to one of the two groups of 30 patients each. Group O patients received injection Ondansetron 4mg and Group P patients received injection Palonosetron 75mcg intravenously 15 minutes before induction. All episodes of PONV within 72 hours after induction of anaesthesia were recorded.

Statistical Analysis: Statistical analysis was done using two sample t test.

Results: The incidence of complete response (no PONV, no rescue medication required) during 0-6 hours in post-operative period was 93.33% in patients of group O and 86.67% in patients of group P. But the incidence of complete response during 6-24 hrs of post-operative period was only 73.33% in patients of group O while it was 93.33% in patients of group P. During 24-48 hours in postoperative period incidence of complete response was only 66.67% in group O while it was 96.67% in group P. And during 48-72 hrs in postoperative period incidence of complete response was 86.67% in patients of group O and 96.67% in patients of group P. Rescue antiemetic in the form of inj. Metoclopramide was given in the patients who had vomiting.

Conclusion: Single dose of Palonosetron was more effective for prevention of nausea and vomiting in comparison to Ondansetron after 6 hrs in post-operative period in abdominal surgeries.

Keywords: PONV, Abdominal surgery, Ondansetron, Palonosetron.

INTRODUCTION

PONV is one of the most unpleasant side effects which can affect the patients after surgery and it is often the worst memory of their hospital stay. Incidence of PONV is very high in abdominal surgeries and especially female patients are at high risk.^{1,2} Patients report that avoidance of Postoperative Nausea and Vomiting is of great concern than avoidance of postoperative pain.³

Ondansetron was the first serotonin antagonist used in chemotherapy induced nausea and vomiting.^{4,5} Ondansetron is a carbazole derivative which is structurally related to serotonin and possess specific subtype 5-HT₃ receptor antagonist properties, without altering dopamine, histamine, adrenergic or cholinergic receptor activity. As a result, it is free of neurologic effects in contrast to droperidol and metoclopramide.⁶ In July 2003, the US Food and Drug Administration approved palonosetron hydrochloride for the treatment of chemotherapy induced nausea and vomiting (CINV).⁷ The newer agent in the class of 5-HT₃ receptor antagonists, palonosetron differs from other agents in its class by its higher receptor-binding affinity thus

selectively blocks serotonin from binding to these receptors peripherally and centrally. When compared with other agents in the class, palonosetron exhibits a longer half-life (40 hours) and has a greater 5-HT₃ receptor binding affinity.⁸ Nausea is defined as a subjectively unpleasant sensation associated with an urge to vomit. Retching is defined as the laboured, spasmodic, rhythmic contraction of the respiratory muscles, including the diaphragm, chest wall and abdominal wall muscles without expulsion of gastric contents. Vomiting is defined as the forceful expulsion of gastric contents from the mouth brought about by the powerful sustained contraction of the abdominal muscles, descent of diaphragm & opening of gastric cardia.⁹ Complete response (CR) was defined as no post-operative retching, no vomiting, and no need of rescue medicines.¹⁰

We designed this prospective randomized double blind study to assess and compare the antiemetic efficacy of Ondansetron and Palonosetron to prevent PONV in patients undergoing elective abdominal surgery under general anaesthesia and to

compare the side effects and complications of this drug.

METHODS

The study protocol was approved by institutional ethical committee and informed consent was taken from every patient. Sixty female patients of ASA Grade 1 and 2, aged 20-40 years who were scheduled for various abdominal surgery under general anaesthesia were included in this study. They were randomly assigned to one of the two groups containing 30 patients each.

All patients were thoroughly examined pre-anaesthetically based on history, physical examination, chest x-rays and other laboratory investigations. Pregnant and lactating females, patients with huge abdominal mass, or undergoing chemotherapy/radiotherapy, on hormonal supplements, patients of motion sickness and previous history of PONV, history of smoking, full stomach, and patients having gastro-oesophageal, cardiorespiratory, renal, hepatic disease, hypersensitive to 5-HT₃ antagonist were excluded from the study.

All the patients were kept fasting 6-8 hours and injection Pantoprazole 40 mg was given in 100 ml NS i.v. slowly a night before the day of surgery. In the operation theatre, intravenous line was started and basic monitors in the form of ECG, NIBP, and pulse oximetry were connected to the patient. Baseline pulse, BP and SpO₂ were monitored. In a double-blind manner, patients were randomly divided into two groups (30 patients each), received either:

Group O – Ondansetron 4mg in 2ml

Group P – Palonosetron 75 mcg in 2ml

All drugs were injected intravenously 15 minute prior to induction of anaesthesia. As pre-anaesthetic medication inj glycopyrrolate 0.2mg, inj midazolam 0.04mg/kg and inj nalbuphine 10mg were given i.v. to all patients. After preoxygenation for 3 minute, inducing agent inj propofol 2 mg/kg i.v. was given slowly followed by inj succinylcholine 2mg/kg i.v. and IPPV with 100% oxygen and intubation with proper size of endotracheal tube was done after complete muscle relaxation. Maintenance of anaesthesia was done with 1-1.5% isoflurane and vecuronium for muscle relaxation and patients were mechanically ventilated. At the end of surgical procedure, residual neuromuscular block was adequately reversed using intravenous glycopyrrolate 0.4mg and neostigmine 2.5mg. Patients were extubated after complete reversal when patient started breathing spontaneously with adequate tidal excursion and then shifted to post anaesthesia care unit. Pulse, BP and SpO₂ were recorded in postoperative period at 0, 6, 24, 48 and 72 hrs of

surgery. For post-operative pain management, only inj. Diclophenac sodium 75 mg thrice a day and SOS was given intravenously.

All patients were observed for emetic episode and adverse effects for first 72 hrs after recovery from anaesthesia and were recorded during periods of 0-6, 6-24, 24-48 and 48-72 hours. Adverse reactions in duration of 72 hours were also recorded.

Each episode of nausea was treated conservatively and no antiemetic was given. Each emetic episode of was treated with inj. Metoclopramide 10 mg as rescue antiemetic.

STATISTICAL ANALYSIS

Two sample t-test was applied to compare complete response in both groups. p value < 0.05 was considered to be significant. Data were presented as a mean and standard deviation, number and percentage.

RESULTS

Mean age and weight for Group O (ondansetron) was 29.87 years and 56.97 kgs and for Group P (palonosetron) was 31.83 years and 58.30 kgs. The incidence of complete response during 0-6 hrs in postoperative period was 93.33% in patients of Group O and 86.67% in patients of Group P. Comparing the complete response rate there was no significant difference in Group O and P (p value > 0.05) for first 6 hrs of post-operative period.

In 6-24hrs of post-operative observation period 73.33% in patients of Group O and 93.33% patients in Group P showed complete response. Group P showed higher complete response rates than Group O but the difference was not significant statistically (p value > 0.05). In 24-48hrs of post-operative period 66.67% in patients of Group O and 96.67% in patients of Group P had complete response. Group P showed significantly higher complete response rate as compared to Group O (p value < 0.05). In 48-72 hrs post-operative period 86.67% in patients of Group O and 96.67% in patients of Group P showed complete response. (Table 1)

The incidence of nausea in patients of Group O was 10% and in patients of Group P was 3.33% during 0-6 hrs (statistically comparable incidence in all study groups, p value > 0.05). After that no episode of nausea (0%) was recorded in patients of Group P, whereas during 6-24 hrs 6.67% patients had nausea in Group O (p value > 0.05) and during 24-48 hrs 6.67% in patients of Group O had nausea (p value > 0.05). After 48 hrs no patients had nausea. Incidence of headache was 20% in patients of Group O and 13.33% in patients of Group P (p value > 0.05) and incidence of constipation was 6.67% in patients of Group O and 10% in patients of Group P (p value > 0.05). (Table 2).

OBSERVATION TABLE

Table 1: Incidence of Nausea, Vomiting and Complete Response

Time interval	Nausea/ vomiting/ CR	Group O	Group P	p value
0-6 h	Nausea	3(10%)	1(3.33%)	0.197
	Vomiting	2(6.67%)	4(13.33%)	0.668
	Complete response	28(93.33%)	26(86.67%)	0.668
6-24 h	Nausea	2(6.66%)	0	-
	Vomiting	8(26.67%)	2(6.67%)	0.083
	Complete response	22(73.33%)	28(93.33%)	0.083
24-48 h	Nausea	2(6.66%)	0	-
	Vomiting	10(33.33%)	1(3.33%)	0.008
	Complete response	20(66.67%)	29(96.67%)	0.008
48-72 h	Nausea	0	0	-
	Vomiting	4(13.33%)	1(3.33%)	0.350
	Complete response	26(86.67%)	29(96.67%)	0.350

Complete response: Defined as no post-operative retching, no vomiting, and no need of rescue medicines.

Table 2: Incidence of Adverse Complaints in Different Groups

	Group O		Group P		p value
	No	%	No	%	
Headache	6	20%	4	13.33%	0.315
Constipation	2	6.67%	3	10%	0.856

DISCUSSION

PONV is one of the most distressing experience associated with surgery and many patients find it troublesome than post-operative pain itself. The occurrence of intractable vomiting can prolong the hospital stay¹⁴ and hence the economic implications also assume great significance.

The strategies for the prevention of early & late PONV have changed considerably over the last decade, with the focus having moved from single drug therapy to combination antiemetic therapy, or balanced antiemesis. More recently, multimodal management strategies incorporating changes in anaesthetic technique, aggressive fluid management and pain relief strategies have produced even better results.¹⁵

Keith A. Candiotti et al¹⁰: compared palonosetron 75mcg with placebo on the incidence and severity of PONV in patients for 72 hrs after surgery. They noted complete response rate in 0-24 hrs was in 36% of patients in placebo group and 56% in patients of palonosetron 75mcg group (p value <0.001), whereas in present study when complete response rate were calculated in same time interval, it was found that in palonosetron group 90% patients had complete response (p value <0.001%). Complete response rate in 24-72 hrs in above study was 50% in placebo group and 70% in palonosetron 75mcg group (p value=0.002), whereas in present study complete response rate in same time interval in palonosetron group was in 96.67% patients (p value <0.05).

Bhattacharjee D P et al¹¹ conducted a comparison between Palonosetron and Granisetron to prevent PONV after Laproscopic Cholecystectomy. Their results revealed 90% complete response rate in patients who received palonosetron in duration of 0-3h, 3-24h and 24-48h, whereas in this present study complete response rate with palonosetron group was 86.67% patients in 0-6h, 93.33% patients in 6-24h and 96.67% patients in 24-48h.

Park SK, Cho EJ et al¹² compared ondansetron 8mg and palonosetron 75mcg for the duration of 24h and observed that the incidence of PONV was 42.2% in palonosetron and 66.7% in ondansetron group over 24h, whereas we found that the incidence of PONV was 11.67% in palonosetron and 25% in ondansetron group in first 24h. So we also found a higher incidence of PONV in group ondansetron as compared to palonosetron over first 24h but the overall incidence of PONV was lower in their respective groups.

We obtained slightly higher complete response than Bhattacharjee D P et al.¹¹ and Park S K, Cho EJ et al¹² which may be because of type of surgery (higher incidence of PONV in laparoscopic surgeries in their studies¹³). Besides this, we used inj. Pantoprazole 40 mg i.v. night before surgery as premedication and avoidance of use of any opioid analgesic in post-operative period which also contributed in reducing PONV.

CONCLUSION

On the basis of results obtained, it was concluded that in early post-operative period (0-24h) complete response rate in ondansetron and palonosetron was comparable. In delayed post-operative period (24-48 h), palonosetron was superior to ondansetron for complete response. During 48-72 h all the study groups showed comparable complete response rates. Palonosetron was superior to ondansetron in controlling nausea over 72h. So it is concluded that "single dose of palonosetron is better drug to prevent the PONV as compared to ondansetron because of longer duration of action up to 72 hours."

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