Original Research Paper

Volume - 13 | Issue - 03 | March - 2023 | PRINT ISSN No. 2249 - 555X | DOI : 10.36106/ijar

Anaesthesiology

COMPARISON OF THE EFFICACY OF PALONOSETRON VERSUS ONDANSETRON AND DEXAMETHASONE IN PREVENTION/REDUCTION OF POSTOPERATIVE NAUSEA AND VOMITING AFTER ELECTIVE SURGERIES DONE UNDER GENERAL ANAESTHESIA

P K Dileep	Senior resident, Department of Anaesthesiology, Bangalore Medical College and Research Institute, Bengaluru.
Shreyas S Bhat	Senior resident, Department of Anaesthesiology, Bangalore Medical College and Research Institute, Bengaluru.
Charan Raj T K	Junior resident, Department of Anaesthesiology, Mandya Institute of Medical Sciences, Mandya.
Divakar S R*	Assistant professor, Department of Anaesthesiology, Mandya Institute of Medical Sciences, Mandya.*Corresponding Author

ABSTRACT **Background:** Palonosetron, a newer 5-HT3 receptor antagonist has recently been introduced and has a longer half-life and a better safety profile when compared to the older generation 5-HT3 receptor antagonists such as ondansetron. With this background, the present study was conducted with the objective to compare the efficacy of injection palonosetron, and injection ondansetron and injection dexamethasone combination in reducing Postoperative Nausea and Vomiting after Elective Surgeries. **Methods:** A single blinded randomized study was conducted among 100 subjects undergoing elective surgeries under general anaesthesia for a period of 1 year from Jan 2019 to Dec 2019. 50 patients were randomised in to 2 groups Group P (received inj. Palanosetron 0.075 mg intravenously) and Group OD (received inj. ondansetron 4mg and inj. dexamethasone 8mg intravenously). SPSS software 22 version was used to analyse the data. Independent t test and Chi-square test were the tests of significance. P value < 0.05 was considered statistically significant. **Results:** Incidence of emesis at 1 hr, 2hr, 3hr, 4hr and 24 hr in Group P was 8%, 4%, 10%, 14% and 4% and in Group OD was 30%, 32%, 36%38% and 18% respectively. Similarly incidence of episodes of retching at 1 hr, 2hr, 3hr, 4hr and 24 hr in Group P was 8%, 8%, 16%, 22% and 6% and in Group O was 24%, 36%, 42%, 36% and 20% respectively. There was significant difference in incidence of nausea and vomiting between two groups. **CONCLUSIONS:** Palonosetron Was More Effective In Reduction Of Postoperative Nausea And Vomiting After Elective Surgeries Compared To Ondansetron And Dexamethasone With Lesser Side Effects.

KEYWORDS : Palonosetron, Ondansetron and Dexamethasone, PONV

INTRODUCTION

Following the inception of General anaesthesia in the first half of the nineteenth century the phenomenon of postoperative nausea and vomiting (PONV) has challenged postoperative care. John Snow in the 1840s recognized and pioneered the management of this entity 1. Despite the advances in surgical technique and anaesthetic technique the incidence of PONV has remained high. The incidence of PONV has been higher for certain procedures such as laparoscopic cholecystectomies and gynaecological surgeries2. Unresolved PONV may result in prolonged post anesthesia care unit stay and unanticipated hospital re-admission that result in a significant increase in overall health care cost3. PONV is influenced by numerous factors, which may be patient related, surgery related, and anesthesia related factors. Different antiemetics, a combination of the same and even acupuncture has been in use to treat this distressing problem. Guidelines have been published in order to better define and manage this condition.4

Ondansetron is considered as the "gold standard" of treatment when compared with the other antiemetics. The combination of ondansetron with dexamethasone has been found to be highly effective in the reduction of PONV 5,6. However, ondansetron has to be administered thrice daily when used alone and the addition of dexamethasone may be deleterious in diabetics as this may hamper optimum glycemic control. Palonosetron, a newer 5-hydroxytryptamine 3 (5-HT3) receptor antagonist that has recently been introduced and has a longer half-life and a better safety profile when compared to the older generation of 5-HT3 receptor antagonists such as ondansetron7. There is limited literature comparing the efficacy of palonosetron with ondansetron and dexamethasone, especially when comparing laparoscopic surgeries.

Our study was designed to assess and compare the efficacy of two drug regimens, palonosetron and ondansetron with dexamethasone in patients undergoing elective surgeries done under general anaesthesia. A prospective randomized trial comparing the above-mentioned drugs was therefore constructed. The primary outcome that was studied was to compare the incidence of PONV between the two arms. Secondary objectives such as need for rescue antiemetic, dosage time of administering the same and the complications if any were studied.

A wide variety of prophylactic antiemetic regimens have been used for the prevention of PONV. Many of the traditional antiemetics produce undesirable side effects and have limited efficacy. Therefore, the search for more ideal compounds has continued.

MATERIAL AND METHODS

This is a Randomized double-blind comparative clinical study. Patients undergoing elective surgeries under general anaesthesia at Mandya Institute of Medical Sciences and Teaching Hospital, Mandya among100 Patients undergoing elective surgeries under general anaesthesia

INCLUSION CRITERIA:

1. Patients belonging to ASA grade I and II.
2. Patients posted for elective surgeries under general anaesthesia.
3. Patients between the age group 18-60 years.
4. Patients who give informed consent.

EXCLUSION CRITERIA:

1. Patients with known hypersensitivity or contra-indications to study drugs
2. Patients with Body mass index more than 30.
3. Received anti-emetic drugs or drugs with anti-emetic property during 24 hours before anaesthesia.
4. Patients with history of motion sickness.
5. Patients with history of gastro-esophageal reflux disease.

METHOD OF DATA COLLECTION:

As observed over a period of three months in the anaesthesia department, 8-10 elective surgeries were done under general anaesthesia per month. Patients selected for the study were randomly allocated into 2 groups of 50 each by random number table, prepared by another anaesthetist not otherwise involved in the study, outside the operating room, namely:

- Group P: will receive inj. Palonosetron 0.075 mg intravenously.
- Group OD: will receive inj. ondansetron 4mg and inj. dexamethasone 8mg intravenously.

Patients were randomized to receive either inj. palanosetron 0.075 mg

i.v or inj. ondansetron 4 mg in combination with inj. dexamethasone 8mg i.v. Inj. palonosetron 0.075 mg was administered in single iv dose with saline solution added to bring the total volume to 5 ml 10min prior to induction of general anaesthesia to subjects in group P

Subjects in group OD were given inj. ondansetron 4 mg and inj. dexamethasone 8mg dose i.v combination 10 min prior to induction of general anaesthesia. Anaesthesia was induced with thiopentone sodium 5mg /kg and tracheal intubation facilitated with inj. Vecuronium bromide 0.1mg/kg. Anaesthesia was maintained with IPPV (Intermittent Positive Pressure Ventilation) using nitrous oxide plus oxygen (65:35) plus 0.6 to 2 % isoflurane in a closed-circuit system and inj. Vecuronium bromide 0.05 mg/kg. Intra-operatively patient was ensured hemodynamically stable and monitored continuously.

The number of episodes of nausea, retching and vomiting and side effects if any was assessed postoperatively for 24h. The above findings were recorded in the following intervals at 0 to 1 hr., 1 to 2 hr., 2 to 3 hr., 3 to 4hr and 4 to 24hr post-operatively.

Statistical analysis

Data was entered into Microsoft excel data sheet and was analyzed using SPSS 22 version software. Categorical data was represented in the form of Frequencies and proportions. Chi-square test was used as test of significance for qualitative data. Continuous data was represented as mean and SD. Independent t test was used as test of significance to identify the mean difference between two quantitative variables. p value (Probability that the result is true) of <0.05 was considered as statistically significant after assuming all the rules of statistical tests.

RESULTS

TABLE 1: MEAN AGE COMPARISON BETWEEN TWO GROUPS

	Group				p value
	Palonosetron		Ondansetron And Dexamethasone		
	Mean	SD	Mean	SD	
Age (years)	37.46	11.925	34.22	11.673	0.173

Mean Age in years in Palonosetron was 37.46 ± 11.93 and in Ondansetron and Dexamethasone group was 34.22 ± 11.67. There was no significant difference in mean Age comparison between the two groups.

Table 2: Sex Distribution between two groups

Count		Group			
		Palonosetron		Ondansetron And Dexamethasone	
		%	Count	%	
Sex	Female	31	62.00%	27	54.00%
	Male	19	38.00%	23	46.00%

X 2 = 0.657, DF = 1, P = 0.418

In Palonosetron, 62.00% were female and 38.00% were male, in Ondansetron and Dexamethasone, 54.00% were female and 46% were male. There was no significant difference in Sex Distribution between the two groups.

Table 3: Incidence of Emesis between two groups at various intervals of followup

		Group				P value
		Palonosetron		Ondansetron And Dexamethasone		
		Count	%	Count	%	
1hr	No	46	92.0%	35	70.0%	0.005*
	Yes	4	8.0%	15	30.0%	
2hr	No	48	96.0%	34	68.0%	<0.001*
	Yes	2	4.0%	16	32.0%	
3hr	No	45	90.0%	32	64.0%	0.002*
	Yes	5	10.0%	18	36.0%	
4hr	No	43	86.0%	31	62.0%	0.006*
	Yes	7	14.0%	19	38.0%	
24hr	No	48	96.0%	41	82.0%	0.025*
	Yes	2	4.0%	9	18.0%	

In the palonosetron group, incidence of emesis at 1 hr was 8%, at 2 hrs was 4%, at 3 hrs was 10%, at 4 hrs was 14% and at 24 hrs was 4%. In Ondansetron and Dexamethasone group, incidence of emesis at 1 hr was 30%, at 2 hrs was 32%, at 3 hrs was 36%, at 4 hrs was 38% and at 24 hrs was 18%. There was significant difference in incidence of emesis between the two groups at all the intervals of follow up.

Table 4: Incidence of Retching between two groups at various intervals of followup

		Group				P value
		Palonosetron		Ondansetron And Dexamethasone		
		Count	%	Count	%	
1hr	No	46	92.0%	33	66.0%	0.001*
	Yes	4	8.0%	17	34.0%	
2hr	No	46	92.0%	32	64.0%	0.001*
	Yes	4	8.0%	18	36.0%	
3hr	No	42	84.0%	29	58.0%	0.004*
	Yes	8	16.0%	21	42.0%	
4hr	No	39	78.0%	32	64.0%	0.123
	Yes	11	22.0%	18	36.0%	
24hr	No	47	94.0%	40	80.0%	0.037*
	Yes	3	6.0%	10	20.0%	

In the palonosetron group, incidence of retching at 1 hr was 8%, at 2 hrs was 8%, at 3 hrs was 16%, at 4 hrs was 22% and at 24 hrs was 6%. In Ondansetron and Dexamethasone group, incidence of retching at 1 hr was 34%, at 2 hrs was 36%, at 3 hrs was 42%, at 4 hrs was 36% and at 24 hrs was 20%. There was significant difference in incidence of retching between the two groups at all the intervals of follow up.

Table 5: Incidence of Nausea between two groups at various intervals of followup

		Group				P value
		Palonosetron		Ondansetron And Dexamethasone		
		Count	%	Count	%	
1hr	No	44	88.0%	32	64.0%	0.005*
	Yes	6	12.0%	18	36.0%	
2hr	No	46	92.0%	32	64.0%	0.001*
	Yes	4	8.0%	18	36.0%	
3hr	No	41	82.0%	30	60.0%	0.015*
	Yes	9	18.0%	20	40.0%	
4hr	No	38	76.0%	31	62.0%	0.130
	Yes	12	24.0%	19	38.0%	
24hr	No	45	90.0%	41	82.0%	0.249
	Yes	5	10.0%	9	18.0%	

In the palonosetron group, incidence of nausea at 1 hr was 12%, at 2 hrs was 8%, at 3 hrs was 18%, at 4 hrs was 24% and at 24 hrs was 10%. In Ondansetron and Dexamethasone group, incidence of nausea at 1 hr was 36%, at 2 hrs was 36%, at 3 hrs was 40%, at 4 hrs was 38% and at 24 hrs was 18%. There was significant difference in incidence of nausea between the two groups at all the intervals of follow up.

Table 6: Grading of control of emesis over 24hrs Distribution between two groups

		Group			
		Palonosetron		Ondansetron And Dexamethasone	
		Count	%	Count	%
Grading of control of emesis over 24hrs	Complete Control	37	74.00%	13	26.00%
	Nearly Complete Control	13	26.00%	17	34.00%
	Partial Control	0	0.00%	19	38.00%
	Failure	0	0.00%	1	2.00%

X 2 = 32.053, DF = 3, P = < 0.001*

In Palonosetron, 74.00% had Complete Control, 26.00% had nearly to complete control.

In Ondansetron and Dexamethasone, 26.00% had Complete Control, 34.00% had nearly to complete control, 38% had partial Control and 2% had Failure.

There was a significant difference in Grading of control of emesis over 24hrs Distribution between the two groups.

Table 7: Efficacy Distribution between two groups

		Group			
		Palonosetron		Ondansetron And Dexamethasone	
		Count	%	Count	%
Efficacy	Effective	46	92.0%	18	36.0%
	Non Effective	4	8.0%	32	64.0%

4X 2 = 34.02, DF = 1, P = < 0.001*

In Palonosetron, 92.00% had Effective and 8.00% had Non Effective outcome. In Ondansetron and Dexamethasone, 36% had Effective and 64% had Non Effective outcome. There was a significant difference in Comments Distribution between two the groups.

DISCUSSION

In Palonosetron group, 74.00 % had complete control, 26.00 % had nearly to complete control of emesis. In Ondansetron and Dexamethasone group, 26.00 % had complete control, 34.00 % had nearly to complete control, 38 % had partial control and 2 % had failure of control of emesis. There was significant difference in control of emesis over 24 hrs distribution between the two groups. In terms of patient satisfaction Palonosetron group had efficacy of 92.00 % and Ondansetron and Dexamethasone group had 36 %. There was significant difference in Comments Distribution between the two groups.

Our study is in agreement with a study by Kim et al.[7] They have observed lower 4% incidence of vomiting with palonosetron when compared with 18% with ondansetron. The incidence of vomiting observed in palonosetron group was much lower than ondansetron with dexamethasone group in our study.

Our study also correlates well with Singh et al.[8] compared palonosetron to placebo, Ramosetron, granisetron, and ondansetron in a meta-analysis involving adult undergoing elective surgery under general anaesthesia and concluded that palonosetron is as safe as and more effective than placebo, ramosetron, granisetron, and ondansetron in preventing delayed PONV. For early PONV, it has higher efficacy over placebo, granisetron, and ondansetron, which correlates with our study results.

When compared as rescue medication by Keith et al.[9] in a randomized multicentric trial, palonosetron and ondansetron in patients who have already received first-generation 5-HT3 antagonist ondansetron as prophylaxis, there was no difference between primary efficacy endpoints between groups, while palonosetron group showed less emesis in 0–72 h interval.

Kovac et al. [10] in a multicenter, randomized, double-blind study compared three doses of palonosetron with placebo on incidence of PONV in patients for 72 hours after surgery. They concluded that a single dose of 0.075 mg IV palonosetron effectively reduced the severity of nausea and delayed the time to emesis in the inpatient surgical setting. They also found that lower doses were not effective this result correlates with our study where a single dose of 0.075mg IV palonosetron was used. Comparison of use of palonosetron and ondansetron as rescue antiemetic medication in patients receiving first generation 5 HT3 antagonists showed no significant difference in primary efficacy end points between two groups while palonosetron group showed less emesis in 0-72 hrs interval.

Amit Kumar et al. [11] in their study observed that vomiting was significantly higher in group A (palonosetron 0.05mg) (37.3%) as compared with group B (21.3%) at 0–48 hours (P = 0.031). Significantly more patients in Group A had nausea as compared with group B (palonosetron 0.075mg) at 90–120 minutes (30.66% vs 18.66%, P = 0.043) and 6–24 hours (32.0% vs 22.66%, P = 0.029). The findings were similar to the present study.

Srivastava VK, et al. [12] in their study observed that the incidence difference for nausea was statistically significant between groups O and P at a time interval of 2to 6 hours only (p = 0.026). The incidence and severity of vomiting were not statistically significant between groups O and P during the whole study period. The overall incidence of postoperative nausea and vomiting (0-24 hours postoperatively) was 37.5% in group O and 9.4% in group P (p = 0.016). The frequency of rescue medication was more common in group O than in group P patients (p = 0.026). Our study results correlate with their results which showed that palonosetron was more effective in preventing / reducing PONV in the early 2-6 hrs period than at 24 hrs.

Similar results to our study was obtained in the study conducted by Sharma S et al. [13] who found out the incidence of PONV (P = 0.002), nausea (P = 0.0002) and vomiting (P = 0.006) was significantly lower in palonosetron group than in ondansetron group in 2- to 12-hour period. QTc interval prolongation, a known side effect of ondansetron was not found in palonosetron group intraoperatively.

Our results showed good agreement with the consensus guidelines that palonosetron is an alternative to ondansetron and dexamethasone. The fact that palonosetron can be administered as a single dose during the surgery and that it can be administered to patients with endocrine abnormalities such as diabetes (dexamethasone may impair glycemic control) is an added benefit. It is also known to have a better safety profile than ondansetron as QT prolongation is not seen with this newer drug.

CONCLUSION

Palonosetron was more efficacious than ondansetron in controlling emesis, nausea and retching in post-surgical patients undergoing general anaesthesia. Overall efficacy was high for Palonosetron compared to Ondansetron and Dexamethasone group. Palonosetron was found equally safe as Ondansetron. In the Palonosetron group, 8 %, 4 %, 10 %, 14 % and 4% at 1, 2, 3, 4 and 24 hrs respectively had emesis and in Ondansetron and Dexamethasone group, 30 %, 32 %, 36 %, 38 % and 18% at 1, 2, 3, 4 and 24 hrs respectively had emesis. There was a significant difference in emesis and number of episodes distribution between the two groups from 1hour to 4 hours.

REFERENCES

1. Islam S, Jain P. Post-operative nausea and vomiting (PONV). Indian J Anaesth. 2004 Jul 1;48(4):253–253.
2. Apfel CC, Heidrich FM, Jukar-Rao S, Jalota L, Hornuss C, Whelan RP, et al. Evidence-based analysis of risk factors for postoperative nausea and vomiting. Br J Anaesth. 2012 Nov 1;109(5):742–53.
3. Fortier J, Chung F, Su J. Unanticipated admission after ambulatory surgery--a prospective study. Can J Anaesth J Can Anesth. 1998 Jul;45(7):612–9.
4. Gan TJ, Diemunsch P, Habib AS, Kovac A, Kranke P, Meyer TA, et al. Consensus guidelines for the management of postoperative nausea and vomiting. AnesthAnalg. 2014 Jan;118(1):85–113.
5. Song JW, Park EY, Lee JG, Park YS, Kang BC, Shim YH. The effect of combining dexamethasone with ondansetron for nausea and vomiting associated with fentanyl-based intravenous patient-controlled analgesia. Anaesthesia. 2011 Apr;66(4):263–7.
6. Ahsan K, Abbas N, Naqvi SMN, Murtaza G, Tariq S. Comparison of efficacy of ondansetron and dexamethasone combination and ondansetron alone in preventing postoperative nausea and vomiting after laparoscopic cholecystectomy. JPMA J Pak Med Assoc. 2014 Mar;64(3):242–6.
7. Kim J, Napadow V, Kuo B, Barbieri R. A combined HRV-fMRI approach to assess cortical control of cardiovagal modulation by motion sickness. ConfProcAnnuIntConf IEEE Eng Med BiolSoc IEEE Eng Med BiolSocAnnu Conf. 2011; 2011:2825–8.
8. Singh PM, Borle A, Gouda D, Makkar JK, Arora MK, Trikha A, et al. Efficacy of palonosetron in postoperative nausea and vomiting (PONV) – A meta-analysis. J Clin Anesth 2016; 34:459-82.
9. Singh P, Yoon SS, Kuo B. Nausea: a review of pathophysiology and therapeutics. TherAdvGastroenterol. 2016 Jan;9(1):98–112.
10. Kovac AL, Eberhart L, Kotarski J, Clerici G, Apfel C; Palonosetron 04-07 Study Group. A randomized, double-blind study to evaluate the efficacy and safety of three different doses of palonosetron versus placebo in preventing postoperative nausea and vomiting over a 72-hour period. Anesth Analg 2008; 107:439-44
11. Kumar A, Solanki SL, Gangakhedkar GR, Shylasree TS, Sharma KS. Comparison of palonosetron and dexamethasone with ondansetron and dexamethasone for postoperative nausea and vomiting in postchemotherapy ovarian cancer surgeries requiring opioid-based patient-controlled analgesia: A randomised, double-blind, active controlled study. Indian J Anaesth 2018; 62:773-9.
12. SrivastavaVK,etal.Comparisonofpalonosetron-dexamethasonea n d ondansetrondexamethasone for prevention of postoperative nausea and vomiting in middle ear surgery: a randomized clinical trial. Rev Bras Anestesiol. 2020.
13. Sharma S, Khanna S, Das J, Mehta Y, Handa KK. A randomized study to compare palonosetron with ondansetron for prevention of postoperative nausea and vomiting following middle ear surgeries.J Anaesthesiol Clin Pharmacol 2019;35:182-7.