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Comparative Study of Anti - Emetic Efficacy of Palonosetron with Ondansetron And Metoclopramide

KEYWORDS: Palonosetron, PONV, antiemetics

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ABSTRACT *Aim:*

This study was designed to assess the safety and efficacy of palonosetron in comparison with ondansetron and metoclopramide administered intravenously before general anesthesia for prevention of post operative nausea and vomiting.

Patients and methods:

A randomized prospective study was carried out in 60 patients aged 18-65 yrs of ASA grade I, II and III. They were categorized into 3 groups. Group P (n = 20) received Inj: palonosetron 0.25mg, Group O (n = 20) Inj: ondansetron 4 mg and Group M (n = 29) Inj: metoclopramide 10 mg.

Results:

Statistically, no significant difference was found in the anti-nausea efficacy of palonosetron compared to ondansetron and metoclopramide. Comparing overall incidence of vomiting showed that the antiemetic efficacy of palonosetron is the same as ondansetron and metoclopramide for post-operative emesis.

INTRODUCTION

Post operative nausea and vomiting (PONV) continues to be a highly undesirable outcome of anesthesia and surgery. It is a limiting factor in the early discharge of ambulatory surgery patients and is a leading cause of unanticipated hospital admission. PONV can lead to an increased recovery room time, expanded nursing care and increase total health care costs. Equally important are the high levels of patient discomfort and dissatisfaction associated with PONV. The incidence of PONV has recently decreased by almost 50%, because of a change in anaesthesia to non-opioid or supplemented opioid premedication, lighter and non-ether anaesthesia, refinement of operative technique and identification of emetogenic factors[1,2,3].

Over the years, numerous drugs have been used in the management of PONV like the phenothiazines, butyrophenone droperidol, dopamine antagonist metoclopramide and recently the 5-HT3 antagonists. Ondansetron and palonosetron decrease chemotherapy induced emesis and also act as a potentially useful prophylaxis for PONV. These drugs are also used for the prevention of PONV[5,6].

This study was conducted to compare the efficacy of palonosetron 0.25mg intravenous, ondansetron 4mg IV and metoclopramide 10mg IV in the control of postoperative nausea and vomiting after general anaesthesia for short surgical procedures and to study the newly discovered and recently study proven effect of palonosetron to prevent PONV.

MATERIALS AND METHODS

The efficacy and safety of i.v palonoseteron, i.v. ondansetron and i.v. metoclopramide were evaluated and compared for prevention of postoperative nausea and vomiting in a randomized double blind placebo controlled study, at Kasturba Medical College Hospitals, Mangalore.

Patient selection: After obtaining approval from institutional human ethics committee and written informed consent, 60 patients [ASA grade I, II & III aged between 18-65 years] undergoing short surgical procedures were enrolled for the study. Any patient having a history of acid peptic disease or hepatic dysfunction, with previous history of PONV or any antiemetic medications, history allergy, history of chronic cough, and history of motion sickness were excluded from study.

Patients were explained the procedure, and were randomly allocated into three groups to receive:- Group P (n = 20) Inj: palonosetron 0.25mg, Group O (n = 20) Inj: ondansetron 4 mg and Group M (n = 29) Inj: metoclopramide 10 mg. After nil per oral for 8-10hrs, all patients underwent a standardized anaesthesia protocol. All the study agents were introduced intravenously prior to starting of procedure. Premedication was with Inj. midazolam 1mg and induction with Inj: thiopentone, propofol or ketamine in titrated doses and maintainence with N_2O in O2. Vitals were monitored throughout, and after the procedure patients shifted to postoperative ward when fully awake and monitoring continued.

Nausea was defined as an unpleasant sensation of a desire to vomit, not associated with expulsive muscular movement. Vomiting was defined as the forceful expulsion of even a small amount of upper gastrointestinal contents through the mouth.

Emetic episodes (nausea and / or vomiting) experienced by patients were recorded in the immediate postoperative (0-2 hours) and delayed postoperative (2-24hours) periods in the post-operative ward by an anaesthesiologist who was blinded to the antiemetic treatment the patient had received.

If one or more episodes of emesis occurred in each observation period, inj. ondansetron 4mg IV was administered as

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rescue antiemetic to the patient.

Statistical analysis:
preformed by using chi- square and fisher 'f' probability test.

OBSERVATIONS AND RESULTS:
A total of 60 patients of ASA grade I, II and III were categorized into 3 groups. Group P received IV palonosetron 0.25mg , Group O IV ondansetron 4mg and Group M IV metoclopramide 10mg.

The results of fisher 'f ' test of comparison of age, sex, ASA grading is shown in following tables. p value of less than 0.05 was considered as significant.

Table1: Age incidence in different groups

AGE

	N	Mean Age	Std. Deviation	Minimum	Maximum
Inj. Palanosetron 0.25mg i.v.	20	45.5500	13.88098	22.00	63.00
Inj. Ondansetron 4mg i.v	20	38.2000	13.98721	20.00	65.00
Inj. Metoclopramide 10mg i.v.	20	43.3000	13.89472	23.00	60.00

a. F=1.464 p=.24 ns

Ages of the patients in the three groups were statistically similar.

Table2: Sex distribution in different groups

SEX * GROUP

			GROUP			Total
			Inj. Palanosetron 0.25mg i.v.	Inj.Ondansetron 4mg i.v	Inj. Metoclopramide 10mg i.v.	
SEX	F	Count	15	8	17	40
		%	75.0%	40.0%	85.0%	66.7%
	M	Count	5	12	3	20
		%	25.0%	60.0%	15.0%	33.3%
Total		Count	20	20	20	60
		%	100.0%	100.0%	100.0%	100.0%

a. x2=10.05 p=.007 hs

The above table shows that the incidence of nausea and vomiting was significantly higher among female patients as compared to male patients.

Table3: ASA grading in different groups:

ASAGRADE

		GROUP			Total
		Inj. Palanosetron 0.25mg i.v.	Inj.Ondansetron 4mg i.v	Inj. Metoclopramide 10mg i.v.	
I	Count	6	14	9	29
	%	30.0%	70.0%	45.0%	48.3%
II	Count	6	5	0	11
	%	30.0%	25.0%	.0%	18.3%
III	Count	8	1	11	20
	%	40.0%	5.0%	55.0%	33.3%
Total	Count	20	20	20	60
	%	100.0%	100.0%	100.0%	100.0%

a. X2=16.916 p=.002 hs

ASA grading in the three groups shows that the incidence of PONV was significantly higher in the ASA grade I patients, who were probably stronger and healthier.

Incidence of Nausea / vomiting during 0 – 2 hours and 2 – 24 hours post-operative:

Table 4: Immediate postoperative nausea during 0 – 2 hours:

			GROUP			Total
			Inj. Palanosetron 0.25mg i.v.	Inj.Ondansetron 4mg i.v	Inj. Metoclopramide 10mg i.v.	
	Absent	Coun	20	19	20	59
		%	100.0%	95.0%	100.0%	98.3%
	Present	Count	0	1	0	1
		%	.0%	5.0%	0%	1.7%
Total		Count	20	20	20	60
		%	100.0%	100.0%	100.0%	100.0%

a. x2=2.034 p=.362 ns

Table5: Immediate postoperative vomiting during 0 – 2 hours:

			GROUP			Total
			Inj. Palanosetron 0.25mg i.v.	Inj.Ondansetron 4mg i.v	Inj. Metoclopramide 10mg i.v.	
	.00	Count	20	18	19	57
		%	100.0%	90.0%	95.0%	95.0%
	1.00	Count	0	2	1	3
		%	.0%	10.0%	5.0%	5.0%
Total		Count	20	20	20	60
		%	100.0%	100.0%	100.0%	100.0%

a. x2=2.105 p=.349 ns

Table6: further postoperative nausea during 2 - 24 hours:

			GROUP			Total
			Inj. Palanosetron 0.25mg i.v.	Inj.Ondansetron 4mg i.v	Inj. Metoclopramide 10mg i.v.	
	.00	Count	19	16	18	53
		%	95.0%	80.0%	90.0%	88.3%
	1.00	Count	1	4	2	7
		%	5.0%	20.0%	10.0%	11.7%
Total		Count	20	20	20	60
		%	100.0%	100.0%	100.0%	100.0%

a. x2=2.264 p=.322 ns

Table7: further postoperative vomiting during 2 - 24 hours:

			GROUP			Total
			Inj. Palanosetron 0.25mg i.v.	Inj.Ondansetron 4mg i.v	Inj. Metoclopramide 10mg i.v.	
	.00	Count	19	17	17	53
		%	95.0%	85.0%	85.0%	88.3%
	1.00	Count	1	3	3	7
		%	5.0%	15.0%	15.0%	11.7%
Total		Count	20	20	20	60
		%	100.0%	100.0%	100.0%	100.0%

a. x2=1.294 p=.524 ns

Statistical analysis of the incidence of nausea and vomiting in the three groups was preformed by using chi- square and fisher 'f' probability test.

Nausea: Incidence of immediate postoperative nausea (0-2hrs) in group P was 0% (0/20)
compared to group O and group M which were 5% (1/20) and 0% (0/20) respectively.

Incidence of postoperative (2-24hrs) nausea in group P was 5% (1/20), group O 20%

(4/20), group M 10% (2/20) respectively.

Statistical analysis showed that there is no significant difference in the anti-nausea efficacy of palonosetron, when compared to ondansetron and metoclopramide.

Vomiting: The incidence of immediate postoperative (0-2hrs) vomiting in group P was 0% (0/20), group O 10% (2/20) and group M 5% (1/20).
Incidence of late postoperative (2-24hrs) vomiting in group P 5% (1/20), group O 15%

(3/20) and group M was 15% (3/20).

Comparing the overall incidence of vomiting in the 24-hour post-operative period, it was seen that the antiemetic efficacy of palonosetron is the same as that of ondansetron and metoclopramide.

Incidence of side effects of the antiemetic drugs - headache, dizziness and constipation in the three groups, showed no statistical significance.

DISCUSSION:
A randomized prospective study was carried out in 60 patients aged 18 – 65 years belonging to ASA grade I, II and III, undergoing short surgical procedures. Patients were randomly allocated into 3 groups, and received either

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palonosetron 0.25mg (group P) or

ondansetron 4mg (group O) and metoclopramide 10mg (group M) intravenously before

general anaesthesia.

The result of this study demonstrates that there is no significant difference in the anti-nausea and antiemetic efficacy of palonosetron, when compared to the older and cheaper drugs ondanosetron and metoclopramide. Perhaps the only advantage of palonosetron is the convenience of once-daily dosing, as demonstrated by the higher but still not statistically significant incidence of late post-operative vomiting in the shorter-acting metoclopramide cohort (Group M).

Age-wise occurrence of nausea / vomiting was found statistically insignificant.

Sex distribution - the incidence of post-operative nausea and vomiting was significantly higher in female patients as compared to male patients. This finding is comparable to other recent studies on PONV.

ASA grading – incidence of nausea and vomiting was significantly higher in ASA grade I patients. This could have been due to the stronger post-operative tone / reflexes in these healthier patients, or because the higher ASA grade patients may have been better optimized or anaesthetized.

The side effect profile was similar in the three groups, and there was no significant difference in the occurrence of major side effects with any of the three drugs.

SUMMARY AND CONCLUSION:

From the results of our study, we found that prophylactic administration of palonosetron, ondansetron and metoclopramide for post-operative nausea and vomiting showed no significant difference in the anti-nausea and antiemetic efficacy of palonosetron as compared to ondanosetron and metoclopramide[7,8].

Palonosetron seems to have a prolonged effect in reducing the severity of nausea and vomiting, a feature not shared by other $5HT_3$ antagonists[9].

There was also no difference in the incidence of side effects (headache and dizziness) with palonosetron when compared to metoclopramide and ondansetron.

The magnitude of effect against PONV of palonosetron appears to be similar to that of other older and less expensive drugs, with a similar safety profile. Perhaps the only benefit of using palonosetron is the convenience of once-daily dosing.

Other recent studies too have shown the equal efficacy of metoclopramide to prevent or reduce post-operative nausea and vomiting when compared to palonosetron. Palonosetron may improve the control of nausea and vomiting into the second and third days post-operatively, an effect that may be most marked after major operations requiring inpatient stay. Palonosetron also reduces the severity of delayed nausea, which may be of particular relevance to the day-surgery population for whom it is difficult to identify those at risk of post-discharge PONV and for whom early return to normal activities is important.

However the magnitude of effect against PONV appears to be similar to that of other established drugs following inpatient surgery, and modest against delayed PONV in ambulatory surgical patients, so more evidence is required before a definite role against post-discharge PONV in the day-care setting for palonosetron can be recommended.

REFERENCE

1. Camu F, Lanwers MH, Verbessem D. Incidence and aetiology of post-operative nausea and vomiting. Eur J Anaesthiol 1992;9(suppl 6):25-31. | 2. G.N.C Kenny. Risk factors for PONV. Anaesthesia 1994,vol 49, 6-10. | 3. Burtles R, Peckett B W. postoperative vomiting: some factors affecting its incidence. British Journal Anaesthesia 1957;29:114-23. | 4. Kapur PA: The big "little problem". Anaesthesia Analg 1991;73:243-245. | 5. P.G.Rabey and G.Smith. Anaesthetic factors contributing to PONV. BJA 1992;69(S1) 40-45. | 6. Sinclair DR, Chung F, Mezei G. Can post-operative nausea and vomiting be predicted? Anaesthesiology 1992;91:109-118. | 7. AF Malins, JM Field, PM Wesling, GM Cooper. Nausea and vomiting after gynaecological laparoscopy: comparison of premedication with oral ondansetron, metoclopramide and placebo. British Journal of Anaesthesia 1994;vol 72, no 2:231-233. | 8. I.Henzi, B.Walder and M.R. Tramer. Metoclopramide in the prevention of post-operative nausea and vomiting: a quantitative systematic review of randomized, placebo-controlled studies. British Journal of Anaesthesia 1999;83(5):761-71. | 9. Chelly J., Melson, Pollock J, et al: Oral RS-25259 prevents postoperative nausea and vomiting following laparoscopic surgery. Anaesthesiology 1996a; 85:A21. |