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Original Article

Anaesthesia Section

Comparative Study of Ondansetron and Palonosetron for Prevention of Nausea and Vomiting Following Upper Abdominal Surgeries under General Anaesthesia: A Randomised Control Trial

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ABSTRACT

Introduction: Postoperative Nausea and Vomiting (PONV) is a common entity following surgical procedure. It may result into serious complication like aspiration of gastric contents, prolonged recovery period. Palonosetron is a selective serotonin antagonist that is 5HT3 receptor antagonist with little to no affinity for other receptors and has a longer duration of action. Ondansetron is also a 5HT3 receptor antagonist with shorter duration of action and some side effects.

Aim: To compare the effectiveness of ondansetron and palonosetron for the prevention of PONV following upper abdominal surgeries.

Materials and Methods: This prospective single-blind study included 120 patients randomly assigned to the palonosetron group (n=60) or the ondansetron group (n=60). Using the chi-square test and calculating p-value, the two groups were compared.

Results: The incidence of nausea, vomiting and use of rescue antiemetic was significantly less in palonosetron group as compared to ondansetron group.

Conclusion: From the study, it can be concluded that palonosetron at a dose of 0.075 mg is safe, with lesser side effects and proved more effective than ondansetron 4 mg in prevention of PONV.

Keywords: Adverse effect, Antiemetic, Postoperative

INTRODUCTION

Postoperative Nausea and Vomiting (PONV) is defined as nausea, retching, or vomiting occurring in Post Anaesthesia Care Unit (PACU) or 24-hours following a surgical procedure [1]. PONV are common problems of general as well as regional anaesthesia and a leading cause of delayed discharge and unanticipated hospital admission after surgical procedure. Overall incidence is 30%, but in certain high risk patients it can be as high as 80% [2]. Various studies have already been done and suggest wide variation in overall incidence [3-6]. PONV is frequent in abdominal surgery. Hence, the use of potent antiemetic becomes important to treat it effectively [7].

A study by Apfel CC et al., described nausea as the desire to vomit without the presence of expulsive muscular movements [8,9]. Vomiting is described as pre-set events of motor and autonomic response that results in forceful expulsion of gastric content through the mouth as described by the study of Hasler WL and Chey WD [10]. Retching is the term used to describe the labored, rhythmic respiratory activity, and abdominal musculature contractions that usually precedes vomiting as described in the study of Hasler WL and Chey WD [10]. Retching along with expulsion of gastric content is counted as vomiting [11].

Palonosetron is a second generation serotonin 5HT3 receptor antagonist. Palonosetron exhibited allosteric binding to 5HT3 receptor [12]. It also inhibit neurokinin-1 receptor and produces antiemetic property [13].

A 5HT3 receptors antagonist is used to prevent PONV in the patients undergoing abdominal surgeries under general anaesthesia. FDA has approved the use of Palonosetron for prophylaxis of PONV in 2008.

Palonosetron has an indirect effect by its allosteric binding with 5HT3 receptors [14]. This may be the clinical site of action of the 5HT3 receptor antagonists. Half-life of ondansetron is 3.5 to 5.5 hours and that of palonosetron is 40 hours [15]. IV palonosetron 0.075 mg is found to be more potent than 0.025 mg and 0.050 mg in preventing PONV [16,17].

Many studies have been conducted to evaluate safety and efficacy of antiemetics in a specific groups undergoing particular type of surgery but there are insufficient data available on upper abdominal surgeries cases. To bridge this gap this randomised single blind study was conducted to compare the antiemetic effect and assess the safety of palonosetron (750 mcg) against ondansetron (4 mg) on population covering all eligible postoperative candidates undergoing general anaesthesia with upper abdominal surgeries.

The novelty of the study is that it will further strengthen the hypothesis regarding effect of palonosetron drug in upper abdominal surgeries which has been compared with the popular used intravenous antiemetic ondansetron.

MATERIALS AND METHODS

Present randomised single blind study was conducted on 120 patients between 18 to 65 years of age, who were scheduled for abdominal surgeries under general anaesthesia, in Jawaharlal Nehru Medical College, Acharya Vinoba Bhave Rural Hospital, Sawangi, Wardha, Maharashtra, India, between August 2018 to August 2019.

Sample size was derived using software openepi.com. For the sample size of the two groups, the power was set at 80% (β=0.2) with a 30% reduction of PONV incidence. The significant level was set as 5% (α=0.05, two-tailed). The calculated sample size was minimum 42, so taking potential drop-outs into consideration; the sample size was set as 60 for each group.

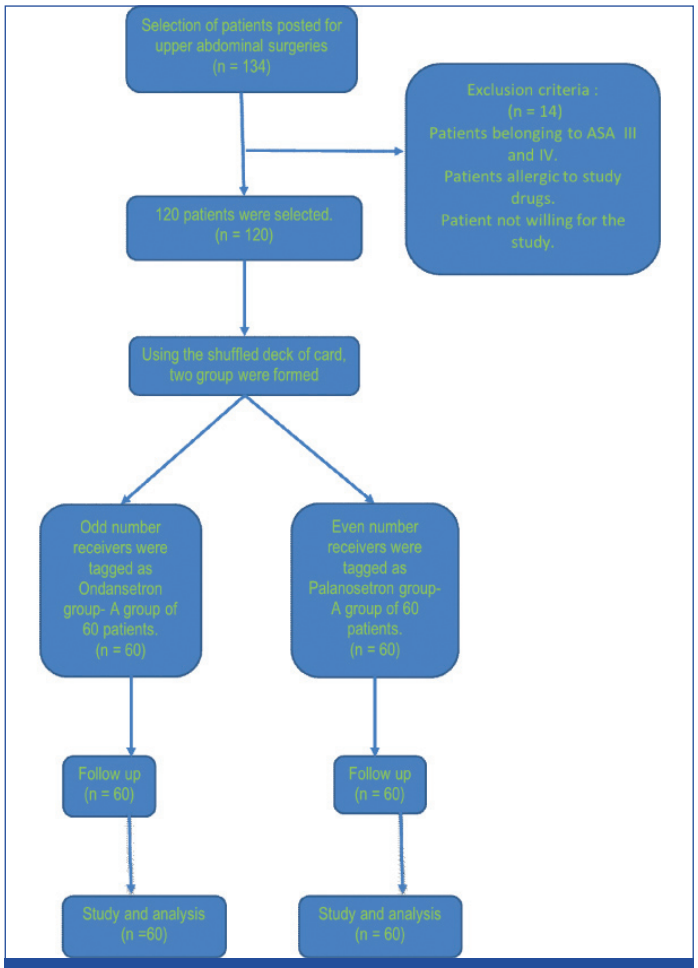
After getting ethical committee approval letter {RefNo. DMIMS(DU)/IEC/2019/7947}, patients were selected randomly after taking

informed written consent. After selection, patient was randomly allocated into two groups, 60 in each, by card sampling. Using the shuffled deck of cards, even number cards were tagged for one group and odd number cards were tagged for other group. Group I received inj ondansetron (4 mg) while group II received inj palonosetron (0.075 mg). Both drugs were given postoperatively before extubation.

Inclusion/Exclusion Criteria

Patients with ASA class I and II, age between 18 to 65 years, weight between 50-80 kg were included. Patients belonging to ASA III and IV, allergic to study drugs were excluded.

A study medication (2 mL) was prepared by one of the investigators and was administered. Thus, two groups of 60 patients each were formed where the researchers were unaware of the group distributed to him/her. Group A (n=60) received ondansetron 2 mL (4 mg), and group B (n=60) received 0.075mg of palonosetron, 2 minutes before injecting reversal. The anaesthetic regimen and surgical procedure was standardised for all patients. Premedication with opioid and sedation (midazolam) and glycopyrolate was given. Intravenous propofol 2 mg/kg was given to patient and anaesthesia was induced. For intubation 0.1 mg/kg vecurnium was used. Anaesthesia was maintained with sevoflurane. Ventilation was controlled mechanically. At the end of surgery after stopping sevoflurane and nitrous oxide, i.v inj. palonosetron (750 mcg) or inj ondansetron (4 mg) was given. Patient was reversed with neostigmine 2.5 mg and glycopyrolate 0.5 mg to reverse residual neuroparalytic block. Tracheal tube was removed after complete reversal and clearing the throat by suction. After surgery, the patients were sent to PACU. Blood pressure, heart rate, and respiratory rate were monitored. Emetic episodes were assessed immediately after operation and at 1 hour interval for 24 hours. Patients with complain of nausea, vomiting, or retching were administered injection dexamethasone 8 mg as a rescue antiemetic [Table/Fig-1].



[Table/Fig-1]: Consort flowchart.

STATISTICAL ANALYSIS

The parameters and patient data were recorded and entered in Microsoft Excel sheet. (SPSS Inc. Chicago, IL, USA) version 20.0 software for windows was used for analysis. Incidence of PONV were compared in two study groups and the results were analysed by using chi-square test. The p-value <0.05 was considered to be significant.

RESULTS

All patients were comparable according to gender, age, bodyweight, duration of anaesthesia and surgery [Table/Fig-2].

Gender	Group A Ondansetron	Group B Palonosetron	p-value
Male	58	63	0.60
Female	62	57	0.60
Age (Yrs.)	34.7±10.3	36.36±10.44	0.38
Wt. (KG)	66±10 kg	68±8 kg	0.22
Duration of anaesthesia	120±45 min	130±30 min	0.15
Duration of surgery	120±45 min	130±30 min	0.15

[Table/Fig-2]: Demography and duration of procedure.

[Table/Fig-3] represent the distribution of open surgeries and laparoscopic surgeries in both groups. There was no significant difference among the two groups.

Type of surgery	Group A Ondansetron	Group B Palonosetron	p-value
Open surgery	32	36	0.58
Laparoscopic surgery	28	24	0.58

[Table/Fig-3]: Type of surgeries.
Open surgeries includes appendectomy, exploratory laparotomy, hemi colectomy, bilateral herniotomy, and cholecystectomy; Laparoscopic surgeries include laparoscopic cholecystectomy, laparoscopic appendectomy, diagnostic laparoscopy, laparoscopic urolithotomy

Incidence of nausea was assessed at the interval of 6 hour up to 24 hours after surgery. Incidence of nausea was found to be significant in first 6 hours, in between 12 to 18 hours among the two groups [Table/Fig-4].

Time	Group 1 Ondansetron	Group 2 Palonosetron	p-value
0-6 hrs	7	0	0.0194 (significant)
6-12 hrs	4	1	0.360
12-18 hrs	6	0	0.0362 (significant)
18-24 hrs	3	1	0.611
Total	20	2	0.0001 (significant)

[Table/Fig-4]: Incidence of nausea in 24 hours.

Retching was significant in first 6 hours and in between 12 to 18 hours among the two groups [Table/Fig-5].

Time	Group 1 Ondansetron	Group 2 Palonosetron	p-value
0-6 hrs	6	0	0.0362 (Significant)
6-12 hrs	3	0	0.242
12-18 hrs	7	0	0.0194 (Significant)
18-24 hrs	4	1	0.360
Total	20	1	0.000185 (Significant)

[Table/Fig-5]: Incidence of retching in 24 hours.

Vomiting was significant in first 6 hours and in between 12 to 18 hours among the two groups [Table/Fig-6].

No significant differences were observed between the groups in adverse effects such as headache, itching and allergic reaction during the first 24 hours after surgery. The p-value remains insignificant as described in [Table/Fig-7].

Time	Group 1 Ondansetron	Group 2 Palonosetron	p-value
0-6 hrs	6	0	0.0362 (significant)
6-12 hrs	2	0	0.4758
12-18 hrs	7	0	0.0194 (significant)
18-24 hrs	6	1	0.1192
Total	21	1	0.0001 (significant)

[Table/Fig-6]: Incidence of vomiting in 24 hours.

Adverse effect in each group	Group A (Ondansetron)	Group B (Palonosetron)	p-value
Headache	6	4	0.1 (Not significant)
Itching	2	1	1 (Not significant)
Allergic reaction	1	0	1 (Not Significant)

[Table/Fig-7]: The incidence of adverse effects in each group.

Severity of postoperative nausea was found to be effective (p-value=0.03) between 12 to 18 hours while severity of postoperative vomiting was found to be effective (p-value=0.01) in between 12 to 18 hours. Overall, the two groups do not have significant differences in reducing the severity of PONV [Table/Fig-8,9].

Blood pressure and pulse rate were noted among ondansetron and palonosetron group. The p-value was insignificant for ondansetron and palonosetron group (p >0.05) as shown in the [Table/Fig-10].

Score	Nausea	Vomiting
0	None	None
1	Mild intermittent nausea	One episode
2	Moderate constant nausea	Several episode
3	Severe nausea	Continuous episode

[Table/Fig-8]: Scoring system for nausea and vomiting [18].

DISCUSSION

In the present study, the antiemetic drugs (ondansetron and palonosetron) were given to the patients just prior to the extubation. Postoperatively, the haemodynamic parameters were noted among the two groups (ondansetron and palonosetron group). It was found that there was no significant difference between the mean values of measured haemodynamic parameters in two study groups [Table/Fig-10]. This observation was similar to study conducted by Paventi S et al., [19].

This study showed that palonosetron was well tolerated and found to be clinically effective in terms of retching, nausea and vomiting (p<0.05) [Table/Fig-4-6]. Recently, there have been studies comparing the effects of palonosetron and other 5HT3 receptor antagonists for the prevention of PONV, sharing similar findings with present study [3,20,21]. The study done by Singhal DM and Sharma N demonstrate that overall incidence of PONV were less as compared to other antiemetic drugs [22,23]. The study done by Moon YE et al., also states that palonosetron is a better drug than ondansetron in preventing PONV [24]. The present study support strongly to the evidence that palonosetron has a potent antiemetic activity within first 6 hours. No significant difference was found between ondansetron and palonosetron in reducing the severity of nausea and vomiting [Table/Fig-9]. This finding was supported by the study conducted by Aydin A et al., [3]. Also, there was no notable difference in side effects among both the groups. Similar finding are found in the study conducted by De Leon A where they compared the adverse effects of ondansetron, palonosetron and dolasetron and stated that adverse reaction were similar in all three groups [25].

Postoperative nausea score					Postoperative vomiting score				
Duration	Nausea score	Ondansetron group	Palonosetron group	p-value	Duration	Vomiting score	Ondansetron group	Palonosetron group	p-value
0-6 hrs.	0	53	60	0.01*	0-6 hrs.	0	54	60	0.03*
	1	5	0	0.06		1	5	0	0.06
	2	0	0	0.92		2	0	0	0.92
	3	2	0	0.47		3	1	0	1.0
6-12 hrs.	0	56	59	0.36	6-12 hrs.	0	58	60	0.47
	1	3	1	0.61		1	2	0	0.47
	2	0	0	0.92		2	0	0	0.92
	3	1	0	1.0		3	0	0	0.92
12-18 hrs.	0	54	60	0.03*	12-18 hrs.	0	53	60	0.01*
	1	6	0	0.03*		1	7	0	0.01*
	2	0	0	0.92		2	0	0	0.92
	3	0	0	0.92		3	0	0	0.92
18-24 hrs.	0	57	59	0.6	18-24 hrs.	0	54	59	0.11
	1	3	1	0.6		1	6	1	0.11
	2	0	0	0.92		2	0	0	0.92
	3	0	0	0.92		3	0	0	0.92

[Table/Fig-9]: PONV score according to duration.
The symbol "*" denotes the significant difference among the two groups

Variables	Ondansetron		Palonosetron		p-value
	Mean	Standard deviation	Mean	Standard deviation	
Systolic blood pressure	107.705	11.014	106.393	11.551	0.525
Diastolic blood pressure	76.885	11.334	75.573	12.045	0.540
Pulse rate	80.918	5.532	80.754	6.168	0.153

[Table/Fig-10]: Comparison of haemodynamic variation among groups.

The present study also showed that p-value for ondansetron and palonosetron group is highly significant in terms of preventing nausea. This finding of the study is also supported by the study Naguib M et al. [26]. Aydin A et al. studied and compared ondansetron, palonosetron and tropisetron for preventing PON, PONV. As stated in their study, the incidence of PONV was less in palonosetron group [3].

Limitation(s)

Equipotent doses were not used. Instead optimal dose were used for comparison. Also the cost of the palonosetron was

much more as compared to ondansetron in Indian market. Many corporate hospitals can afford to use the drug palonosetron instead of ondansetron. But the government institutions of developing countries can find it difficult to use the palonosetron.

CONCLUSION(S)

In conclusion, bolus of intravenous palonosetron 0.075 mg was found to be more efficacious than bolus of intravenous ondansetron 4 mg especially during the first six hours.

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