ORIGINAL RESEARCH

Comparison of palonosetron and ondansetron for prevention of post operative nausea and vomiting in laparoscopic surgeries

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Received: 22 june , 2023 Accepted: 25 july, 2023

Abstract
Introduction: Postoperative nausea and vomiting (PONV) is a common complication of surgery and anaesthesia. PONV have adverse consequences like: prolonged recovery, hospital readmission, delayed ambulation, disruption of surgical sutures, anxiety and increased perception of pain. Aim of this study is to evaluate the role of ondansatron and palonosetron in prevention of postoperative nausea and vomiting in laparoscopic surgeries under general anaesthesia.
Material and Methods: Prospective, randomized, comparative study. After approval from the Institutional Ethical Committee, the study was conducted on 60 patients of either sex, aged 20-75 yrs, of ASA grade I and II and scheduled for elective laparoscopic surgeries under general anaesthesia.. Patients were randomly allocated in two groups: **Group A** – patients who received i.v.ondansetron 4 mg, **Group B** – patients who received i.v.palonosetron 0.075 mg.
Results: Thirty patients received i.v.ondansetron 4 mg grouped as Group A, another thirty patients received i.v.palonosetron 0.075 mg grouped as Group B. The two drugs Palonosetron is better than Ondansetron for prevention of nausea and vomiting as there is decreased incidence of post operative nausea and vomiting is seen with Palonosetron.
Conclusion: The concluded in the study Palonosetron is better than Ondansetron for prevention of nausea and vomiting as there is decreased incidence of post operative nausea and vomiting is seen with Palonosetron.
Keywords: Palonsetron, Ondasetron, Post Operative Nausea, Vomiting

Introduction
Postoperative nausea and vomiting (PONV) is a common complication of surgery and anaesthesia. PONV have adverse consequences like: prolonged recovery, hospital readmission, delayed ambulation, disruption of surgical sutures, anxiety and increased perception of pain.The incidence of PONV in the recovery room and thereafter is 20%, 5% and 50%, 2.5% respectively**(Muchatuta et al 2009**). Activation of the vomiting centre or sensation of nausea may result from stimulation of the chemoreceptor trigger zone (drugs, metabolic stress); vestibular apparatus (motion) visceral afferent inputs (eg. gut distention or stasis, surgical stimulation of viscera, cardiovascular disturbance) cortical inputs (e.g. anxiety, pain, hypoxia, sensory stimuli, psychological association, and raised intracranial pressure). Established factor for PONV are younger age, general anaesthesia, higher intraoperative and postoperative opioid requirement, use of inhalational agent for maintenance rather than propofol, N_2O, inadequate fluid loading, intraoperative hypotension and hypoxemia. $5HT_3$ receptor antagonist is popular and effective drugs for PONV. Ondansetron(2,3,7)is the prototype of a new class of antiemetic drugs developed to control cancer chemotherapy radiotherapy induced vomiting and later found to be highly effective in PONV as well.Palonosetron(1,7) is a newer 5HT3receptor antagonist which is shown to be superior to other 5HT3 receptors. It is a unique $5HT_3$ receptor antagonist having greater binding affinity and longer half life than older $5HT_3$ receptor antagonists like ondansetron. Half life of palonosetron is 40 hrs and of ondansetron is 4 hrs. In this study we compared the efficacy of these two antiemetics (OndansetronvsPalonosetron) in managing PONV in laparoscopic surgeries under general anaesthesia (GA). Aim of this study is to evaluate the role of ondansatron and palonosetron in prevention of postoperative nausea and vomiting in laparoscopic surgeries (2,3) under general anaesthesia.

Materials and methods
Study design: Prospective, randomized, comparative study. After approval from the Institutional Ethical Committee, the study was conducted on 60 patients of either sex, aged 20-

75 yrs, of ASA grade I and II and scheduled for elective laparoscopic surgeries under general anaesthesia. A written and informed consent was taken from patients and their attendents. Patients with history of postoperative nausea and vomiting or motion sickness, patients with diabetes mellitus and pregnant females were excluded from the study.Patients were randomly allocated in two groups: **Group A** – patients who received i.v.ondansetron 4 mg, **Group B** – patients who received i.v.palonosetron 0.075 mg.A thorough medical history was obtained and complete pre-anaesthetic check up of the patient was done. Patients were premedicated with ranitidine 300 mg oral and alprazolam 0.25 mg oral on the night before surgery and on the day of surgery. After taking patient in the operating room, standard monitors including non-invasive blood pressure monitoring, pulse oximetry, temperature and electrocardiogram were applied. An 18 gauge intravenous line was secured and lactated ringer solution was used as intravenous fluid. Study drug was given 15 minutes before induction in each group.In both groups induction was done with propofol 2 mg/kg i.v., if effect is inadequate additional propofol 0.5 mg/kg was given. Fentanyl 2 mcg/kg was used as analgesic. Vecuronium bromide 0.1 mg/kg bodyweight was given for relaxation and patient was intubated after three minutes with cuffed endotracheal tube. 60% N_2O in oxygen and isoflurane was used for maintenance of anaesthesia. Muscle relaxation was maintained with intermittant doses of vecuronium. A nasogasrtic Ryle's tube was placed before starting surgery to decompress stomach. Throughout the surgery patient's heart rate, blood pressure and SpO2 was recorded at every 15 minutes. After completion of surgery, patients were reversed with neostigmine (0.05 mg/kg) and glycopyrrolate (0.01 mg/kg). Ryle's tube suctioned and removed and the patient was extubated. Patients were observed in post anaesthesia care unit for 72 hrs. and vitals were recorded. Incidence of PONV was assessed in postoperative period for 72 hours. Metoclopramide 10 mg. i.v was used as rescue analgesic. Any side effects – headache, constipation, dizziness sedation, hypersensitivity reaction, burning or discomfort at injection site and QTc interval prolongation was noted.

To assess the severity of postoperative nausea and vomiting, scoring system **(Bellville *et al.* ;1959)** was used which was as follows:-

a. No nausea: Score 0
b. Nausea only: Score 1
c. Nausea with retching: Score 2
d. Vomiting: Score 3

The results and data obtained were analysed and subjected to statistical analysis.

Statistical tools employed: The statistical analysis was done using SPSS (Statistical Package for Social Sciences) Version 15.0 statistical Analysis Software. The values were represented in Number (%) and Mean±SD.

Results

Thirty patients received i.v.ondansetron 4 mg grouped as Group A another thirty patients received i.v.palonosetron 0.075 mg grouped as Group B.Table 1 shows that in both the groups majority of patients were aged <41 years. In Group A 63.33% patients and in Group B 80% of subjects were aged <41 years. No statistically significant difference in age of patients of both the groups was found (p=0.444). Furthermore, mean age of Group A patients (39.77±9.49 years) was slightly higher as compared to Group B patients (38.70±8.03 years) but this difference was statistically non-significant (p=0.640). (Table 1)Above data indicate that higher proportion of female subjects (83.33%) were administered Ondansetron (Group A) for antiemesis during surgery as compared to only 73.33% females who were administered Palonosetron (Group B). However, this difference is stastically insignificant (p=0.347). It was also found that in both the groups, proportion of females for laparoscopic cholecystectomy was higher than males. (Table 2)Above data indicate that no statistically significant difference (p=0.848) in body weight of subjects of both the groups was found.At none of the above time periods difference in heart rate of two groups was not found to be statistically significant. Though at baseline systolic Blood pressure of Group B (Palonosetron) subjects (123.27±7.63 mm Hg) was found to be lower than that of Group A (Ondansetron) (127.03±9.26 mm Hg) but this difference was statistically non-significant.Comparison of blood pressure at different time intervals between the two groups revealed that Systolic Blood Pressure in Group A was found to be slightly higher than that of Group B, but difference was statistically significant after time intervals 30 minutes only. At all the time intervals change in systolic blood pressure from baseline values was statistically non-significant in Group B.Difference in mean arterial pressure of both the groups at baseline was statistically non-significant.Difference in mean arterial blood pressure of both the groups was found to be statistically significant at all the above time intervals after 30 minutes.Use of antiemetic was found to be higher in Group A (36.67%) as compared Group B (10.0%) and this difference was statistically significant (p=0.015). (Table 4)Above data indicates that higher proportion of subjects from Group A complained of nausea and vomiting as compared to Group B.(Table 3)Above table shows the score of nausea recorded in all visits was 23. The score of nausea with retching in all visits was 18. The score of vomiting recorded in all visits was found to be 30. Total score of nausea, nausea with retching and vomiting in patients of Group A was 71. (Table 6)Above table shows the score of nausea recorded in all visits was 2. The score of nausea with retching in all visits was 2. The score of vomiting recorded in all visits was found to be 0. Total score of nausea, nausea with retching and vomiting in patients of Group B was 10. This was found to be lower in Group B than Group A (Score 71). (Table 6,Table 7)

Table 1: Distribution of Subjects according to Age

Age Group (years)	Group A (Ondansetron) (n=30)	Group B (Palonosetron) (n=30)	Statistical significance
Mean±SD	39.77±9.49	38.70±8.03	't' value = 0.470 p=0.640
Median	38.50	36.50	
Range	20-59	23-60	

Table 2: Distribution of Subjects according to Gender

Gender	Group A (Ondansetron) (n=30)		Group B (Palonosetron) (n=30)		Statistical significance	
	No.	Percentage	No.	Percentage	χ^2	'p'
Female	25	83.33	22	73.33	0.884	0.347
Male	5	16.67	8	26.67		

Table 3. Post-Operative Nausea and Vomiting at different time intervals

Time Intervals	Group A (Ondansetron) (n=30)		Group B (Palonosetron) (n=30)		Statistical significance	
	No.	Percentage	No.	Percentage	χ^2	'p'
24 hours	10	33.33	3	10.00	4.812	0.028
48 hours	7	23.33	3	10.00	1.920	0.166
72 hours	5	16.67	3	10.00	0.577	0.448

Table 4: Comparison of Use of Rescue Antiemetic in Study Population

Rescue antiemitic	Group A (Ondansetron) (n=30)		Group B (Palonosetron) (n=30)		Statistical significance	
	No.	Percentage	No.	Percentage	χ^2	'p'
No	19	63.33	27	90.00	5.963	0.015
Yes	11	36.67	3	10.00		

Table 5: Comparison of Adverse reactions

Complications	Group A (Ondansetron) (n=30)		Group B (Palonosetron) (n=30)		Statistical significance	
	No.	Percentage	No.	Percentage	χ^2	'p'
Headache	2	6.67	3	10.00	0.218	0.640
Comstipation	2	6.67	2	6.67	0.000	1.000
Diarrhoea	2	6.67	0	0.00	2.069	0.150
Dizziness	2	6.67	0	0.00	2.069	0.150
Fatigue	0	0	0	0	–	–
Abdominal Pain	0	0	0	0	–	–
Insomnia	0	0	0	0	–	–

Table 6: Total Scoring after 24 hours for Group A

Episodes	I (0-2 hrs)	II (2-4 hrs)	III (4-6 hrs)	IV (6-12 hrs)	V (12-24 hrs)	Scores
Nausea	5	6	3	3	6	23 x 1 = 23
Nausea with Retching	5	4	0	0	0	9 x 2 = 18
Vomiting	5	5	0	0	0	10 x 3 = 30
	Total Score = 71					

No Nausea = Score 0; Nausea only = Score 1; Nausea with retching = Score 2; Vomiting = Score 3

Table 7: Total Scoring after 24 hours for Group B

Episodes	I (0-2 hrs)	II (2-4 hrs)	III (4-6 hrs)	IV (6-12 hrs)	V (12-24 hrs)	Scores
Nausea	0	2	0	0	0	= 2 x 1 = 2
Nausea with Retching	0	1	0	0	0	= 1 x 2 = 2
Vomiting	1	1	0	0	0	= 2 x 3 = 6
	Total Score = 10					

No Nausea = Score 0; Nausea only = Score 1; Nausea with retching = Score 2; Vomiting = Score 3

Discussion

Postoperative nausea and vomiting (PONV) is due to stimulation of 5HT3 receptor which are situated on the nerve terminal of the vagus nerve in the periphery and centrally on the chemoreceptor trigger zone of the area postrema.**(Bunce,Tyres,1992,Watcha,1992).** Postoperative period is associated with variable incidence of nausea and vomiting depending on the duration of surgery, the type of anaesthetic agents used (dose, inhalational drugs.opioids) smoking habit etc. Postoperative nausea and vomiting (PONV) (1,2,3) is multifactorial in its origin, that is, as a consequence of emetogenic agents (inhaled anesthetics, opioids) applied to susceptible patients (females, those with a history of motion sickness, nonsmokers); which are associated with an increased incidence of post operative nausea and vomiting (PONV) but also important independent predictors of postoperative nausea and vomiting (PONV). Anaesthetic agent initiate the vomiting reflex by stimulating the central 5HT3 receptors on the chemoreceptor trigger zone receptors and also by releasing serotonin from the enterochromaffin cells of the small intestine and subsequent stimulation of 5HT3 receptors on vagus nerve afferent fibres**(Bunce, Tyres, 1992).** The advantage of laparoscopic surgery (2,3,4) includes reduced postoperative stress response to surgery, rapid return of GI function, reduced postoperative pain and analgesic requirements, improved post operative respiratory function, reduced recovery time, less wound infection and improved cosmetic appearance. We studied the two most commonly used 5HT3 antagonists used in anaesthetic practice and compared there efficacy in reduction of post operative nausea and vomiting.Comparing the characterstics of the

two groups the mean age, percentage of gender, ASA physical status and weight of the two groups were found to be statistically the same *i.e.* did not differed significantly ($p>0.05$). In other words subjects of two groups were age, sex and weight matched. As there is increased incidence of gall stone disease seen in females in comparison to males it was found that in both the group of females for laparoscopic surgery was higher than males. Thus the age, gender, weight and ASA grade may not influence the outcome measures of the study.On comparing heart rate and blood pressures (systolic, diastolic and mean) between the two groups there was no statistically significant difference seen. No significant intragroup heart rate and blood pressure variability was found. On comparing the SpO2 levels of all the subjects in both groups ranged between 96-100, *i.e.* within normal limits. In post operative period the incidence of nausea and vomiting was recorded for upto 72 hours.The first 24 hours was further divided into 0-2 hours, 2-4 hours, 4-6 hours, 6-12 hours, and 12-24 hours. Postoperative nausea and vomiting was further divided into three groups *i.e.* nausea, nausea with retching and vomiting.The incidence of nausea in group A *i.e.* Ondansetron group within 24 hours, 48 hours and 72 hours was 33.33%, 23.33% and16.67% respectively. The incidence of nausea with retching in 0- 2 hours, 2-4 hours, 4-6 hours, 6-12 hours, 12-24 hours 48 hours and 72 hours was 16.67%, 15% and 0% for rest of the time intervals. The incidence of vomiting at 0-2 hours, 2-4 hours was 16.67%, 16.67% and it was 0% at 4-6 hours, 6-12 hours, 12-24 hours, 48 hours and 72 hours. The incidence of nausea in group B *i.e.* Palonosetron group within 24 hours 48 hours and 72 hours was 10% at all the time intervals. Nausea with retching in group B was seen in 6.2% cases at 2-4 hours time interval and its incidence at rest of the time intervals was zero. Not a single episode of vomiting was seen in group B. The incidence of PONV is slightly higher with Ondansetron in first 24 hrs, in our study as compared to previous study in which it was 14%, 7% and 4% at 0-4 hours, 4-12 hours and 12-24 hours. **Chidambaram et al.** Whilethere was decreased incidence of post operative nausea and vomiting with Palonosetron(1,2) group**.**Adverse reactions - In group A *i.e.*ondansetron group there was 6.67% incidence of headache, 6.67% incidence of constipation, 6.67% incidence of diarrhea and 6.67% incidence of dizziness. In group B *i.e.*Palonosetron group there was headache and constipation with incidence of 10% and 6.67%. For control of postoperative nausea and vomiting we used $5HT_3$ antagonists Ondansetron and Palonosetron in premedication. Ondansetron has short half life of 3-5 hours and Palonosetron(7) has half life of 40 hours. Therefore due to longer half lifePalonosetron has longer duration of action than Ondansetron. In our study we also found that Palonosetron was effective for 72 hour for control of postoperative nausea and vomiting. So out of the two drugs Palonosetron is better than Ondansetron for prevention of nausea and vomiting as there is decreased incidence of post operative nausea and vomiting is seen with Palonosetron.

Conclusion

Sixty patients, both male and female between 20-75 years were selected for the study. The incidence of post operative nausea and vomiting in patients undergoing laparoscopic surgeries is quite higher. Ondansetron and palonosetron both are 5HT3 antagonists we used in our study. The incidence of postoperative nausea and vomiting was more in ondansetron than palonosetron group. For control of postoperative nausea and vomiting we used $5HT_3$ antagonists Ondansetron and Palonosetron in premedication. Ondansetron has short half life of 3-5 hours and Palonosetron has half life of 40 hours. Therefore due to longer half lifePalonosetron has longer duration of action than Ondansetron. In our study we also found that Palonosetron was effective for 72 hour for control of postoperative nausea and vomiting. So out of the two drugs Palonosetron is better than Ondansetron for prevention of nausea and vomiting as there is decreased incidence of post operative nausea and vomiting is seen with Palonosetron.

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