



Original Research Article

Comparative study between ondansetron & palonosetron in prevention of post operative nausea vomiting operated under general anaesthesia: A randomised double blind study

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ABSTRACT

Introduction: Postoperative nausea vomiting [PONV] is very common complication in patient undergoing surgery. Despite various medication and patient factors anaesthesiologists continues to face discomfort in preventing PONV. This study compares the incidence of nausea and vomiting during initial 24 h post anaesthesia, need for any rescue medication, satisfaction of patients and incidence of adverse effects between ondansetron & palonosetron.

Methodology: In this study a total 60 patients of ASA I II, scheduled for open cholecystectomy, were selected and double blind randomization done in two groups, which either receive inj ondansetron 4mg or inj Palonosetron 75mcg before initiation of induction of anaesthesia. The events of nausea and vomiting and need of any rescue antiemetic drug was monitored at 0–2, 2–6, 6–24hrs and 0-24hrs after surgery. The visual analogue scale (VAS; 0, no nausea; 10, worst nausea) used to assess severity of PONV. Inj Metoclopramide 10 mg i.v. was administered as a rescue antiemetic. Adverse effects including headaches, dizziness, constipation and myalgia were recorded. Satisfaction on a three-point scale (satisfied, equivocal, dissatisfied) after 24 hr were recorded.

Result: There is increased incidence of nausea & vomiting in ondansetron than palonosetron group at 0-2, 2-6, 6-24 and at 0-24 hrs with significant difference between both groups (p value<0.05). In present study the incidence of adverse effects like presence of new headache, any dizziness, complains of myalgia, constipation were found nearly similar in both groups. In ondansetron group nearly 13% patients needed rescue antiemetic whereas in palonosetron group 7% patients needed rescue antiemetic but the difference was not significant (p value>0.05). After 24 hr of surgery patients in palonosetron group were more satisfied than ondansetron group without any significant difference (p value>0.05).

Conclusion: Effectiveness of Palonosetron in preventing PONV found to be significantly more than that of Ondansetron. Decreased incidence of adverse effects, less need of rescue antiemetic drugs & having more patient satisfaction found in palonosetron group.

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1. Introduction

Postoperative Nausea and Vomiting (PONV) = after anaesthesia continues to be the most commonly encountered complication after anaesthesia inspite of availability of many antiemetic drugs and various regimens for prevention.

J Lance Lichtor quotes in his editorial “we are tired of waiting for the ‘big little problem’ to be solved”.^{1,2} There is incidence of PONV in 30-40% in normal population operated under general anaesthesia, but the incidence rises to 75-80% in few high risk groups.³

Various risk factors which includes female gender, non smokers, h/o motion sickness, nature and duration of surgery and perioperative opioids usage⁴⁻⁶ It has been found

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that presence of anxiety prior to surgery, anaesthetic drugs and technique also affect the incidence of PONV.⁷ A very high incidence of PONV (40-70%) during initial 24 hour in laparoscopic cholecystectomy has been found.^{8,9} Use of nonopoid drugs for pain management has been related to decrease in incidence of PONV.¹⁰ Smokers tends to have favourable profile in incidence of PONV than nonsmokers.

Agents like 5-HT₃ antagonists are used now a days in controlling and preventing PONV. These 5-HT₃ antagonists are as effective as various other antiemetic drugs but with a increased margin of safety and favourable side-effects. 5-HT₃ antagonists which includes ondansetron, granisetron, tropisetron and palonosetron have more favorable drug profile and duration of antiemesis (4-48 hours) (10). Ondansetron is now commonly used 5-HT₃ antagonist in the treatment of post operative nausea and vomiting. Palonosetron, a second generation 5-HT₃ antagonists is potentially a good drug for its use in prevention of PONV.¹¹ It has unique chemical structure, and a significant prolong half life (40 hrs).

This study was formulated to evaluate the effectiveness of palonosetron versus ondansetron in preventing PONV in patients undergoing open cholecystectomy.

2. Materials and Methods

The study was conducted after obtaining approval from the institutional proforma committee of S N Medical College Agra, and written informed consent from the patient. The present study was conducted from Jan 2013 to August 2014 in the department of Anaesthesia & Critical Care, S N Medical College Agra and cases were selected from surgery department. For this study total 60 patients of ASA I II, scheduled for open cholecystectomy, were selected double blind randomization done in two groups, which either receive inj ondansetron 4mg or inj Palonosetron 75mcg before initiation of induction of anaesthesia. All the patients were randomized in two groups.

Group O: 30 patients received inj Ondansetron 4mg iv bolus (n=30).

Group P: 30 patients received inj Palonosetron 75 mcg iv bolus (n=30).

Inclusion/ Exclusion Criteria for Participants in this Trial

2.1. Inclusion criteria

1. Female more than 18 years of age.
2. American Society of Anesthesiologists (ASA physical status I and II).
3. Atleast 2 of the following PONV risk factors.
 - a. Female sex
 - b. History of PONV and or motion sickness
 - c. On smoker
4. Patients undergoing elective open cholecystectomy.

5. General anaesthesia with endotracheal intubation as outlined in the anesthesia procedures section provided in protocol.

2.2. Exclusion criteria

1. Uncooperative & Inability to understand the study procedures as determined by the Investigator.
2. Pregnant, nursing or women planning to become pregnant, are not using effective birth control, or that have had a positive serum pregnancy test within 72 hours prior to surgery.
3. Cancer patients who had undergone chemotherapy within 4 weeks prior to study entry.
4. Any kind of emetogenic radiotherapy within 8 weeks prior to enrolment in study.
5. Has received any investigational drugs < 30 days before enrolment in study.
6. History of any emetogenic drugs taken in last 24 hrs before anaesthesia.
7. Body mass index (BMI >40).
8. Known or suspected current history of alcohol intake.
9. Known hypersensitivity or having contraindication to 5-HT₃ antagonists.
10. History of Epilepsy.
11. Vomiting in last 24 hrs before surgery.

The patients include were randomized to receive either inj palonosetron 75 mcg or inj ondansetron 4 mg intravenously. A computer generated randomization of sealed, numbered envelopes containing drugs was done by qualified physicians not involved in anaesthesia process. Palonosetron 75 mcg in 2 ml dilution was administered in a single i.v. dose prior to induction of anaesthesia to subjects in the palonosetron group. ondansetron group received inj ondansetron 4 mg in single i.v. dose as 2 ml solution.

The patients enrolled were given tablet alprazolam 0.25mg and tablet Ranitidine hydrochloride 150mg orally night before surgery & were explained regarding visual analog scale (VAS) of nausea which ranges from 0 having no nausea to 10 having worst nausea. Selected patients received either inj Ondansetron or inj Palonosetron prior to induction of anaesthesia. Anaesthesia procedures includes pre Oxygenation for 3 minutes with 100% oxygen. Induction done with inj thiopentone Sodium (4-7mg/kg), analgesia with inj fentanyl (1-2 microgms /kg) and injection vecuronium (0.1mg/kg) i/v used as muscle relaxant used to facilitate endotracheal intubation.

Anaesthesia maintained with usage of O₂ +N₂O + isoflurane along with vecuronium 0.02mg/kg as maintenance dose. After commencement of surgery reversal from muscle relaxants done with injection neostigmine (0.05mg/kg) and inj Glycopyrrolate (0.01mg/kg). Duration of general anaesthesia and surgery was noted. Inj diclofenac aq 75 mg i/v injection was given 15 min before extubation for post

operative pain. In postoperative ward pain was controlled by Inj diclofenac aq 75 mg i.v 8th hourly or on patient demand.

The episodes of nausea and vomiting and usage of rescue antiemetic drug were monitored at.

2.3. Monitoring and Observation

Monitoring was done at 4 interval at 0 – 2hrs, 2 – 6hrs, 6 – 24hrs and 0-24hrs after surgery. we monitored any episode of PONV & need of rescue antiemetic drug. Visual analogue scale was used to grade the severity (VAS= 0 no nausea & 10 having worst nausea). We had used Inj Metoclopramide 10 mg i.v. as antiemetic after one episode of vomiting occurred or nausea at VAS>5 or when the patient requested treatment(rescue treatment).

Details of adverse effects including headaches, dizziness, constipation and myalgia were taken. Grading of overall satisfaction was done on a three-point scale which include (satisfied, neutral, dissatisfied) 24 hr after surgery in postoperative ward.

The primary goal of this study was to measure the incidence of nausea and vomiting during the first 24 h after administration of anaesthesia. Secondary goal measured were any need for rescue medication, incidence of adverse effects & overall patient satisfaction.

2.4. Statistical analysis

The statistical observation of the categorical variables were evaluated by using Chi square and student T test for continuous Variables and one-way analysis of variants ANOVA for comparison of mean values among study groups. The observed side effects were analysed with Fisher's exact test. The observational results are expressed mainly as mean \pm SD or number (%). P value <0.05 was considered significant.

3. Results

1. We found that there was increase in episodes of nausea in ondansetron group than palonosetron group at time 0-2, 2-6, 6-24 and at 0-24 hrs and the difference was significant between both the Groups (p value<0.05).
2. The mean age, weight, duration of surgery and the risk factor of PONV were similar in each group and was without any significant difference between both the groups (p value >0.05).
3. We found that there was increase in episodes of vomiting in ondansetron group than palonosetron group at 0-2, 2-6, 6-24 and 0-24 hrs. and the difference was significant between both the Groups (p value<0.05).
4. Results shows that incidence of various side effects like headache, dizziness, constipation, myalgia were similar between both the groups with no significant difference (p value >0.05).

5. Rescue antiemetic usage was more common in ondansetron group than palonosetron 13% vs 7% respectively but result was not significant between both the groups (p value >0.05).

6. Satisfaction level was more in patients in Palonosetron than in Ondansetron group after 24 hr of surgery, but without any significant difference (p value >0.05).

Table 1: Mean age distribution between two groups

	Group O (n=30)	Group P (n=30)	P value
Mean age(in year)	40.77	39.830	.737
S.D.	9.529	11.763	

Both group O (ondansetron group) and group P (palonosetron group) are comparable with each other with respect to age. On statistical analysis p value is 0.737 (p value>0.05). This shows that there is no significant difference in age distribution between two groups

Table 2: Comparison of weight between group O and P

		Group P (n=30)	P value
Mean weight (kg)	47.47	52.03	.09
SD	6.027	6.98	

There is no statistical significant difference between mean weight of two groups. The P value >0.05 (p value=0.09).

Table 3: Comparison of duration of surgery between group O and P

	Group O (n=30)	Group (n=30)	P value
Mean duration of surgery (min)	60.63	60.17	.778
SD	6.014	6.727	

The mean duration of surgery between group O and group P are comparable to each other

Table 4: Comparison of risk factor of ponv between group O and P

Risk factor	Group O	Group P	P Value
PONV	13	14	
None smoking	7	9	.665
PONV+Nonsmoking	10	7	

In both the groups risk factors are comparable. There is no significant difference regarding risk factor in both the groups

Table 5 showing incidence of nausea between group O and Group P at different time intervals.

In ondansetron group nausea incidence is more in comparison. To palonosetron group at different time intervals. On comparison of both groups p value is <0.05 at different time intervals. It means there is significant difference in incidence of nausea in both groups.

Table 5: Comparison of no. of patients having nausea between group O and P at 0-2, 2-6, 6-24, 0-24 hr in postoperative period-

Time(hr)	Group O (n=30)	Group P (n=30)	P value
0-2	10	2	.008
2-6	11	4	.036
6-24	13	7	.046
0-24	19	10	.019

Table 6: Comparison of no. no patients having vomiting episodes between group O and at 0-2, 2-6, 6-24, 0-24 hr in postoperative period

Time(hr)	Group O(n=30)	Group P(n=30)	P value
0-2	6	2	.046
2-6	5	1	.026
6-24	4	1	.038
0-24	9	3	.042

On observation the incidence of vomiting episodes are more Common in group O than group P at different time intervals and the p value is <0.05 at different time intervals. It means there is significant Difference in incidence of vomiting in between two groups.

Table 7: Comparison of side effects between group O and P with in 24 hours of postoperative period

Side effect	Group O(n=30)	Group P(n=30)	P value
Headache	3	2	.500
Dizziness	4	4	.647
Constipation	2	3	.500
Myalgia	0	1	.500

In group O group p the incidence of adverse effects are almost similar and the p value is >0.05 showing that there is no significant difference in incidence of adverse effects between two Groups.

Table 8: Comparison of no. of patients receiving rescue medication between group O and P

	Group O (N=30)	Group P (N=30)	P value
No of patient receiving rescue medication	10	6	.072

Rescue antiemetics use were more common in ondansetron group. Than palonosetron group. But there is no significant difference.

After 24 hrs of post operative period in palonosetron group more patient are satisfied than the ondansetron group and the p value>0.05 showing that there is no significant difference regarding patient satisfaction in between two groups.

Table 9: Subjective assessment of patient's satisfaction between group O and P

Category	Group O (n=30)	Group p (n=30)	P value
Satisfied	16	21	583
Neutral	7	5	

4. Discussion

Postoperative nausea and vomiting (PONV) continues to be common annoying complication following surgery under general anaesthesia. This study compares the incidence of PONV, incidence of adverse effects if any, the need of rescue medication to prevent PONV and to compare patient's satisfaction rate in both the groups.

During initiation of vomiting reflex there is 5-HT 3 receptor stimulation.¹² The central 5-HT 3 receptors are present in the medullary chemoreceptive trigger zone. Anaesthetic agents activates these receptors. They also act on enterochromaffin cells of the small intestine receptors thereby releasing serotonin which subsequently stimulates 5-HT 3 receptors present on vagus nerve afferents.¹³

With this complex etiology and dependence on various variables including age, obesity, a history of previous PONV, surgical procedure, anaesthetic drugs and postoperative pain, preventing PONV is a challenge.¹⁴⁻¹⁷

In this study, the groups were comparable with respect to patient demographics, risk factors and analgesics used postoperatively. Therefore difference in outcome is due drugs under study.

Competitive Inhibition by 5-HT3 receptor antagonists like ondansetron and Palonosetron at peripheral 5-HT3 receptors located in vagal nerve terminals can block triggering of the vomiting reflex by emetogenic stimuli.¹⁸ Receptor binding properties & pharmacokinetics are attributable to differences in between two groups.

Other clinical trials gave insight to select the doses of drugs which was ondansetron 4mg and palonosetron 75mcg.^{19,20} these were single pre-Induction dose with I/V route.

In this study which include total 60 patients with ASA physical status I and II, undergoing open cholecystectomy under general anaesthesia were selected & randomized to two groups, groups O (n = 30) & group P (n = 30) which receives Inj Ondansetron 4 mg i.v. & Inj Palonosetron 75 mcg i.v respectively before initiation of anesthetic administration.

Mean age of patients in the ondansetron group and palonosetron group was 40.77±9.529 yrs, 39.83±11.76 yrs respectively. p value obtained was 0.737 (p >0.05).

Similarly, after comparison of mean weight, mean duration of surgery and risk factor of PONV between group O and group P shows no statistical significant difference (p value>.05).

On comparison of nausea between group O and group P at 0-2hrs, 2-6 hrs, 6-24 hrs, 0-24hrs the incidence of nausea in Ondansetron group O and in Palonosetron group it is 33.3%, 36.6%, 43.3%, 63.3%, is 10%, 13.3%, 23.3%, 33.3% respectively. At these observational intervals the p value is < 0.05 , shows a significant difference between these two groups. Similar results were found in various studies.^{21,22}

In present study on comparison of vomiting between group O and group P at 0-2hrs, 2-6 hrs 6-24 hrs, 0-24hrs, the incidence of vomiting was 20.0%, 16.66%, 13.3% & 30.0% in O group and 6.66%, 3.33%, 3.33% & 10.0% in P group at different time intervals respectively. In all the groups the p value is < 0.05 . It means there is significant difference in incidence if vomiting between two groups. Results were similar as obtained by Y.E. Moon et al which is comparable to our study.²³

On comparing side effects between two groups, in group O vs group P for complained of headache, the p value is 0.50 (> 0.05).

We found that there is no significant difference in the incidence of side effects of 5-HT₃ antagonists like dizziness, constipation and myalgia in two groups.

Inj Metoclopramide 10mg i.v was used as rescue antiemetics in both the groups. There is no significant difference in the use of rescue antiemetics between two groups. However the rescue antiemetic use was more common in ondansetron group.

In group P more patients are satisfied, it means that palonosetron has better control in preventing PONV than Ondansetron

The findings of our study are also consistent with the various studies which shows that palonosetron is more efficacious than ondansetron in prevention PONV.^{21–23}

5. Conclusion

Palonosetron is significantly more effective than ondansetron in preventing post operative nausea and vomiting with decreased incidence of adverse effects, less rescue antiemetic usage & having more patient satisfaction.

6. Source of Funding

None.

7. Conflict of Interest

There are no conflict of interest.

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