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Research Article

Comparison of antiemetic efficacy of palonosetron, ondansetron and granisetron in prevention of postoperative nausea and vomiting

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ABSTRACT

Background: Postoperative nausea and vomiting (PONV) was termed "the big little problem" nearly a quarter century ago in an editorial .The past decade has witnessed the introduction of several significant innovations to combat PONV, but it still remains as big a problem as before because newer choices and confusions over standardization added side by side . The aim of this study is to compare the efficacy of palonosetron with that of granisetron and ondansetron in the treatment and prevention of postoperative nausea and vomiting after laparoscopic cholecystectomy.

Methods: This randomized prospective comparative clinical study was carried out in the NIMS Medical College & Hospital, NIMS University, Jaipur, during the period of January 2013 to December 2013 amongst female patients of ASA grade I and II (ASA = American Society of anesthesiology) , scheduled for laparoscopic cholecystectomy under general anesthesia. A total number of 90 patients were selected and randomized into three groups of 30 patients each. Group-I was given inj. palonosetron (0.25 mg), Group-II was given inj. granisetron (1 mg) and Group‑III was given inj. ondansetron (8 mg). One way analysis of variance (ANOVA) and Pearson's Chi-square test were done as the tests of significance whenever applicable to compare the mean of different groups.

Results: The incidence of nausea was 10% in Palonosetron-group while it was found to be 60% in Ondansetron-group. The incidence of vomiting was 6.7% in group-I, 26.6% in group-II & 53.3% in group-III respectively. The difference was statistically significant between group I vs group II ($p < 0.05$). 13.3% of patients in Palonosetron-group required rescue antiemetic, while in Ondansetron-group, it was 46.7%.

Conclusions: To conclude, palonosetron greatly reduced the incidence of postoperative nausea and vomiting, and also the requirement of rescue antiemetic in postoperative period than granisetron and ondansetron. Patients were satisfied by using this drug. Palonosetron is more effective in comparison to granisetron and ondansetron in the prevention and treatment of postoperative nausea and vomiting after laparoscopic cholecystectomy.

Keywords: Post-operative nausea and vomiting, Palonosetron, Granisetron, Ondansetron

INTRODUCTION

The first surgery under general anesthesia was performed successfully on 16th October, 1846. Post-Operative Nausea and Vomiting (PONV) has first extensive descriptions by Sir John Snow in 1848, within 18 months of chloroform introduction in anesthesia. Since then, in less than 170 years almost, at least 102 editorials have been published in Medline-indexed journals focusing on PONV.[1]

PONV was termed "the big little problem" nearly a quarter century ago in an editorial.[2] The past decade has witnessed the introduction of several significant innovations to combat PONV, particularly the introduction of serotonin antagonists and the use of combinations of drugs for analgesia and control of PONV.[3] But it still remains as big a problem as before because newer choices and confusions over standardization added side by side.[3]

Actually the avoidance of Post-Operative Nausea and Vomiting (PONV) is very important from the patient's perspective[4] - some studies report PONV up to 85%.[5] And this data is here when "PONV in routine clinical care is likely to be underreported".[6]

PONV also has cost implications in terms of nursing time, delayed recovery, hospital resources and possible re-operation costs.[7-9] Thus right now PONV is one of the most common and distressing complication of surgery under general anesthesia[10] and thereby, PONV is still important in epidemiological and financial terms.[11]

A triple comparison of ondansetron, granisetron and metoclopramide is already there[12] but triple comparison among 5-HT3 antagonists is not available. That's why comparing these two against a new entity of palonosetron is the aim of this study.

Aim and objectives

1. To compare the efficacy of palonosetron with that of granisetron and ondansetron in the treatment and prevention of postoperative nausea and vomiting after laparoscopic cholecystectomy.
2. To observe the incidence of nausea and vomiting separately in the postoperative period,
3. To observe the requirement of rescue antiemetic,
4. To find out the haemodynamic stability (heart rate and systolic/ diastolic blood pressure)
5. To detect the patients satisfaction by verbal rating scale after 24 hours of surgery.

METHODS

After taking permission from the institutional ethical committee, this randomized prospective clinical study was carried out in the NIMS Medical College & Hospital, Jaipur, during the period of January 2013 to December 2013.

Inclusion criteria

1. Female patients aged between 30-50 years
2. ASA grade I and II (ASA = American Society of Anesthesiology)
3. Scheduled for laparoscopic cholecystectomy under general anesthesia

Exclusion criteria

1. Females with known history of hypersensitivity to study drugs,
2. Gastrointestinal diseases,
3. Who had taken antiemetics within 24 hours before surgery,
4. Receiving hormonal therapy
5. Pregnant and menstruating patients.

A total number of 90 patients, sex female, age range 30-50 years undergoing laparoscopic cholecystectomy were selected by sequential sampling (automatically randomized by inclusion/exclusion criteria and previously unknown sequence of enrolment for surgery). They were equally divided into three groups of 30 patients.

Group-I was given inj. palonosetron (0.25 mg)[13,14] - as 5 ml vial containing 0.25 mg of the drug was procured and 5 ml of the preparation was used as a single bolus.

Group-II was given Inj. granisetron (1 mg)[15,16] - as 1.0 ml vial containing 1 ml of the drug was procured and was used as a single bolus.

Group-III was given inj. ondansetron (8 mg)[12,17] - as 4 ml vial containing 2 x 4 = 8 mg of the drug was procured and 4 ml of the preparation was used as a single bolus.

Patients' data were collected in prescribed forms containing patients' particulars, preoperative baseline (pulse, blood pressure-systolic and diastolic blood pressure) parameters, preoperative and postoperative parameters including nausea, vomiting, patients' satisfaction by 4 points VRS (Verbal Rating Scale) and use of rescue antiemetics.

Patients were monitored preoperatively and postoperatively. In postoperative room proper hydration was maintained. Analgesia was maintained by injection pethidine (1.5 mg/kg) given intramuscularly 8 hourly in each patient, injection ketorolac (30 mg) intramuscularly was given on patient's demand.

The 24 hours study period started upon entry to the postoperative room. Patients were observed at 30 minutes, 1 hour, 2 hours, 4 hours, 8 hours, 16 hours and 24 hours after recovery.

In this period hemodynamic parameters (pulse, systolic and diastolic blood pressure), arterial oxygen saturation, the number and time of nausea and vomiting and rescue antiemetic treatment were recorded. Injection antiemetic was given according to the patient's need. Patient satisfaction was recorded by 4 points verbal rating scale 24 hours after recovery.

Statistical analysis

All the variables were expressed as mean ± SD. One way analysis of variance (ANOVA) and Pearson's Chi-square (χ^2) test were done as the tests of significance whenever applicable to compare the mean of different groups. The statistical analysis was done by using SPSS program. P-value <0.05 was considered as significant.

RESULTS

Observation of the present study was analyzed in the light of comparison among each subject groups. The groups became statistically matched for age (P=0.948), weight (P=0.908) i.e. there was no significant difference among the study groups as shown in the Table 1.

Nausea

The incidence of nausea was 10% in group-I, 33.3% in group-II & 60% in group-III respectively as shown in Table 2/Figure 1.

Vomiting

As shown in Table 3/Figure 2, the incidence of vomiting was 6.7% in group-I, 26.6% in group-II & 53.3% in group-III respectively. The difference was statistically significant between group I vs. group II (p <0.05).

Patient satisfaction

As shown in Table 4, overall patient satisfaction in 24 hours in post-operative period by Verbal Rating Scale (VRS). After 24 hours overall patient satisfaction was assessed. In group-I, 1 patients rated "not effective at al", 6 "moderate effective", 11 "effective" and 12 "excellent".

Table 1: Age and body weight distribution amongst different study groups (n=90).

Variable	Group-1 (n=30)	Group-2 (n=30)	Group-3 (n=30)	f-statistic	P-value
Age (years)	37.3 ± 2.06	36.7 ± 1.82	37.5 ± 1.49	1.59	> 0.05
Weight (kg)	53.5 ± 1.38	54.4 ± 1.90	54.4 ± 1.88	2.68	> 0.05

Table 2: Incidence of nausea between different study groups (n=90).

Groups	n	No nausea	Nausea	Chi-square value	P value
I (Palonosetron Group)	n=30	27 (90.0%)	3 (10.0%)		
II (Granisetron Group)	n=30	20 (66.7%)	10 (33.3%)	16.632	0.00024p < 0.05.
III (Ondansetron Group)	n=30	12 (40.0%)	18 (60.0%)		
Total	90	59 (62.2%)	31 (34.4%)		

Table 3: Incidence of vomiting in different study group (n=90).

Groups	n	No vomiting	Vomiting	Chi- square value	P value
I (Palonosetron Group)	n=30	28 (93.3%)	2 (6.7%)		
II (Granisetron Group)	n=30	22 (73.3%)	8 (26.7%)	16.0096	0.000334p < 0.05.
III (Ondansetron Group)	n=30	14 (46.7%)	16 (53.3%)		
Total	90	64 (71.1%)	26 (28.9%)		

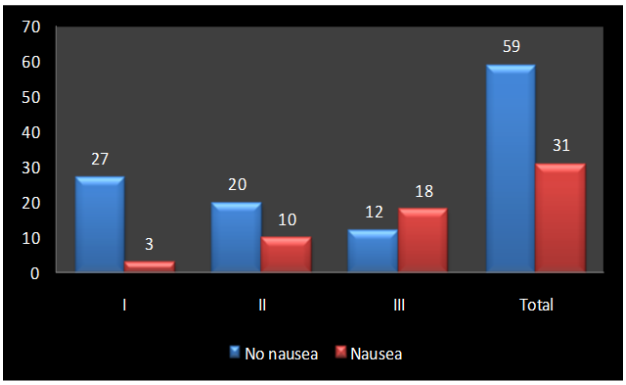

Figure 1: Incidence of nausea between different study groups (n=90).

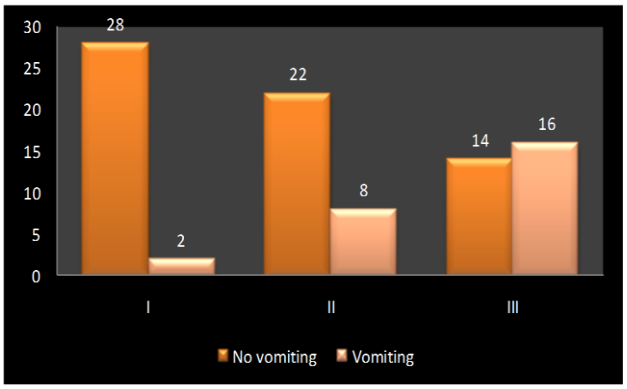

Figure 2: Incidence of vomiting in different study group (n=90).

Table 4: Satisfactory level by verbal rating scale.

VRS	Group I (n=30)	Group II (n=30)	Group III (n=30)	Total (n=90)	χ2 value	P value
Not effective at all	13.3%	516.7%	723.3%	1314.4%		
Moderately effective	620.0%	1033.3%	1343.3%	2932.2%		
Effective	1136.7%	930.0%	723.3%	2730.0%	13.75	0.032s
Excellent	1240.0%	640.0%	310.0%	2123.3%		
Total	30100.0%	30100.0%	30100.0%	90100.0%		

Rescue antiemetic

The incidence of rescue antiemetic in different study groups are shown in number and percentage in Table 5.

Our study found that heart rate difference among the groups at preoperative, intraoperative, postoperative upto 24 hours after recovery were not significant as shown in Table 6.

There was no significant changes in systolic and diastolic pressure among the groups of studied patients as shown in Table 7/8.

Table 5: Rescue antiemetic used in different study groups.

Rescue antiemetic required	Group I (n=30)	Group II (n=30)	Group III (n=30)	Total (n=90)	χ2 value	P value
No	2686.7%	2170.0%	1653.3%	6370.0%		
Yes	413.3%	930.0%	1446.7%	2730.0%	7.937	0.02s
Total	30100.0%	30100.0%	30100.0%	90100.0%		

Table 6: Changes in heart rate in different study groups.

	Pre	Intra	30 min	1 hour	2 hour	4 hour	8 hour	16 hour	24 hour
Group-I	88.0±1.6	88.8±2.4	87.8±1.6	89.2 ±1.8	90.2±1.7	89.0±2.2	91.7±1.9	88.6±1.7	82.8±1.2
Group-II	89.1±3.1	91.8±1.4	91.4±2.3	87.6±1.6	88.0±1.6	92.8±1.3	96.6.0±1.9	85.0±0.8	84.6±1.2
Group-III	87.8±1.5	86.9±1.8	88.0±1.6	87.8±1.4	85.6±0.6	90.0±1.8	93.6±2.2	87.2±1.3	82.2±0.7
F value	0.10	1.731	1.027	0.29	2.678	1.209	1.546	1.921	1.45
P value	0.902ns	0.183ns	0.363ns	0.748ns	0.74ns	0.304ns	0.219ns	0.153ns	0.239ns

Table 7: Variation in systolic BP in different study groups.

	Pre	Intra	30 min	1 hour	2 hour	4 hour	8 hour	16 hour	24 hour
Group-I	119.5±3.3	127.0±4.8	119.3±5.5	116.5±3.3	120.5±2.9	115.0±6.4	126.0±3.2	116.5±3.3	116.0±2.8
Group-II	118.0±3.9	135.0±2.4	124.3±6.0	123.0±2.9	122.0±3.1	129.3±6.5	134.5±3.9	123.0±2.9	120.0±3.3
Group-III	121.0±2.3	130.0±2.2	138.3±5.4	124.0±1.9	122.0±2.2	137.3±6.6	134.0±2.9	124.0±1.9	117.0±2.2
F value	0.22	1.47	3.016	2.19	0.10	2.970	1.98	2.19	0.55
P value	0.804ns	0.235ns	0.056ns	0.119ns	0.905ns	0.057ns	0.144ns	0.119ns	0.581ns

Table 8: Variation in diastolic BP in different study groups.

	Pre	Intra	30 min	1 hour	2 hour	4 hour	8 hour	16 hour	24 hour
Group-I	77.5±2.5	89.5±2.9	81.0±2.5	78.5 ±2.5	81.0±2.4	84.0±1.5	86.2±2.4	77.5±2.2	77.5±1.7
Group-II	81.0±2.9	92.5±1.7	80.5±2.7	79.0±1.5	76.0±2.1	84.5±1.6	87.3±1.0	80.0±2.4	79.0±1.9
Group-III	81.0±1.9	88.0±1.6	89.3±3.4	83.0±1.2	83.5±2.4	85.7±1.6	88.5±1.7	85.0±2.4	79.0±1.3
F value	0.66	1.10	2.979	1.82	2.830	.297	.427	2.618	0.27
P value	0.517ns	0.337ns	0.056ns	0.168ns	0.064ns	0.744ns	0.654ns	0.079ns	0.766ns

DISCUSSION

Nausea and vomiting are among the most common postoperative complaints. These are frequently the cause of great distress to patients and it is often the worst memory of their hospital stay.[18] The consequences of prolonged postoperative nausea and vomiting (PONV) range from unexpected admission of day patients, with its economic implications to physical, metabolic and psychological effect on the patients.[19]

Better anesthetic technique, identification of precipitating factors, use of new generation of antiemetics and improvement in operative techniques reduce the incidence and severity of PONV has been decreasing over the last 10 years. Despite these changes, there is still unacceptable frequency of PONV with incidences up to 85% reported in some studies.[5]

A study suggests that the incidence of postoperative nausea and vomiting has remained constant for decades with 20-30% of patients suffering from these unpleasant side effects.[20] Thus PONV is likely to create considerable extra cost for health care system. The aetiology of PONV is complex and multifactorial. Factors associated with an increased risk of postoperative emesis include age, gender, obesity, a history of motion sickness and/or previous postoperative emesis, anxiety, menstruation, gastroparesis, pain, hypoxia, type of anaesthetic, hypotension and type and duration of the surgical procedure.[21]

Patients undergoing laparoscopic surgery are at high risk for postoperative nausea and vomiting. Because most of them are female and due to instrumental manipulation release of humoral substance include 5-hydroxytryptamine (5-HT) which may stimulate 5-HT receptor in the afferent vagus nerves triggering the emetic reflex chemoreceptor trigger zone and pneumoperitonium needed for laparoscopy has direct effect on postoperative nausea and vomiting.[20]

Yoshitaka Fujii and Hiroyoshi Tanaka[22] studied the efficacy of the selective 5-hydroxytryptamine receptor antagonist granisetron with that of the traditional antiemetics droperidol and metoclopramide in the treatment of established PONV after laparoscopic surgery.[23]

In their study there were no significant group differences in patient's demographic or surgical characteristics. There was no significant difference in haemodynamic parameters - pulse, B.P and saturation of arterial oxygen.[23] The number of patients who were emesis free (no nausea, retching or vomiting) was significantly higher in patients who received granisetron (88%, 22/25), than who received droperidol (60%, 16/25, P=0.047) or metoclopramide (55%, 14/25, P=0.013).[23]

By comparing with this study,[23] our study found that heart rate difference among the groups at preoperative, intraoperative, postoperative upto 24 hours after recovery were not significant. There was no significant changes in systolic and diastolic pressure among the groups of studied patients. The incidence of nausea in group-I 10%, in group-II 33.3% and in group-III - 60.0%. In our study, the incidence of "no nausea" was significantly higher in patients who received palonosetron (90.0%, 27/30) than in those who received granisetron (66.7%, 20/30, P=0.028) or ondansetron (40.0%, 12/30, P=0.000).

The incidence of vomiting in group-I (6.7%). In group-II (26.7%) and group-III (53.3%). In our study, the incidence of "no vomiting" was significantly higher in patients who received palonosetron (93.3%, 28/30) than in those who received granisetron (73.3%, 22/30, P=0.037) or ondansetron (46.7%, 14/30, P=0.000). Also in the study, palonosetron was associated with greater

patients satisfaction than granisetron and ondansetron 40%, 20% and 10% of patients, respectively (P=0.032). No need for another rescue antiemetic medication was achieved in 86.7% of patients with palonosetron, 70.0% with granisetron and 53.3% with ondansetron (P=0.02) in this study.

In the present study, 5 patients were excluded as laparoscopic procedures could not succeed and open cholecystectomy were done. To maintain the postoperative analgesia injection pethidine (1.5 mg/kg) was given intramuscularly 8 hourly and inj. ketorolac (30 mg) was given I/M on demand. In our study, it was a great satisfaction that though injection pethidine was given to all patients of three groups for post-operative analgesia and sedation, there was no increase in frequency of nausea and vomiting episodes as its side effects, which were also probably blocked by inj. palonosetron, granisetron and ondansetron.

Our result showed that, Injection palonosetron (1 mg) administered 10 minutes before reversal of anaesthesia is more effective than granisetron and ondansetron in the prevention and treatment of postoperative nausea and vomiting after laparoscopic cholecystectomy.

CONCLUSION

The present study was particularly designed to observe the incidence of nausea and vomiting and requirement of rescue antiemetic in postoperative period and also detect the patients' satisfaction by verbal rating scale after 24 hours of surgery.

After completion of the study it was found that palonosetron greatly reduced the incidence of postoperative nausea and vomiting, and also the requirement of rescue antiemetic in postoperative period than granisetron and ondansetron.

Patient was satisfied by using this drug. So this present randomized prospective comparative clinical study concluded that palonosetron is more effective in comparison to granisetron and ondansetron in the prevention and treatment of postoperative nausea and vomiting after laparoscopic cholecystectomy.

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