ORIGINAL RESEARCH PAPER
Volume - 10 | Issue - 01 | January - 2021 | PRINT ISSN No. 2277 - 8179 | DOI : 10.36106/ijsr
INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

COMPARISON OF EFFECTIVENESS AMONG ONDANSETRON, PALONOSETRON AND GRANISETRON IN PREVENTING POSTOPERATIVE NAUSEA AND VOMITING FOLLOWING LAPAROSCOPIC CHOLECYSTECTOMY

Anaesthesiology

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ABSTRACT

Postoperative nausea and vomiting (PONV) has been variously described as the "big little problem" the "final therapeutic challenge" for anaesthesiology. The commonest cause of morbidity after anaesthesia and surgery are pain and postoperative nausea vomiting

1. To compare the incidences of PONV following laparoscopic cholecyetectomy in different groups of patients receiving ondansetron, palonosetron and Granisetron.
2. To identify the better strategy for prevention of PONV.

This is a prospective randomized double blinded clinical study. Both patient and observer were blinded to the group allocation. Allocations to three groups were strictly confidential and concealed. One and half year (18 months). Patients undergoing elective laparoscopic cholecystectomy under General Anaesthesia at General Surgery operation theatres of Bankura Sammilani Medical College and Hospital, Bankura The effects of palonosetron, granisetron and ondansetron in preventing PONV (postoperative nausea vomiting) were compared in patients undergoing laparoscopic cholecystectomy and it was found that palonosetron was best and granisetron better in comparison with ondansetron in preventing postoperative nausea and vomiting. Palonosetron provides more effective prophylaxis of early PON (postoperative nausea), late PON (postoperative nausea), and late POV (postoperative vomiting) compared with granisetron and ondansetron. Palonosetron could provide effective prophylactic antiemetic control to prevent PONV after laparoscopic cholecystectomy surgery under general anesthesia.

KEYWORDS

Ondansetron, Palonosetron, Granisetron And Laparoscopic Cholecystectomy

INTRODUCTION

Postoperative nausea and vomiting (PONV) has been variously described as the "big little problem"[1,2], the "final therapeutic challenge" for anaesthesiology. The commonest cause of morbidity after anaesthesia and surgery are pain and postoperative nausea vomiting[3, 4, 5]. Unrelieved pain is a common cause of PONV [6, 7] and opioids used for pain relief also causes PONV[8]. However acute postoperative pain relief and prevention as well as treatment of PONV recently assumed great importance in anaesthesia.

In spite extensive understanding of physiology of nausea and vomiting and abundance of antiemetic medications, certain surgical procedures are associated with unacceptably high incidence of PONV. Laparoscopic surgery is one of them, which is popular for minimal invasiveness but is associated with increased morbidity due to PONV[9]. Factors believed to contribute are:

I) Rigorous compression and decompression of abdomen by surgeon .
II) Irritation of parasympathetic nerve endings in the abdomen.
III) Effect of carbon dioxide on emetic centre.

Although regarded by medical and nursing staff as minor complication of anaesthesia and surgery, nausea and vomiting are the frequent cause of great distress to the patient. In study by Orkin, approximately three quarter of the patients being questioned, rated freedom from nausea vomiting as their most important postoperative requirement12. Patients were willing to accept dysphoria, loss of mental acuity and increased pain, in order to avoid nausea and vomiting. In a questionnaire analysis nausea was second only to failure to wake up, as a reason for fear of general anaesthesia.

Ramosetron is a newer long-acting selective 5-HT3 receptor antagonist. It exhibits a higher affinity toward the serotonin receptors with a slower dissociation, resulting in a longer duration of action. Palonosetron is a unique 5-HT3 receptor antagonist having a greater binding affinity and longer half-life than other 5-HT3 antagonists.

1. To compare the incidences of PONV following laparoscopic cholecyetectomy in different groups of patients receiving ondansetron, palonosetron and Granisetron.
2. To identify the better strategy for prevention of PONV.

MATERIAL AND METHOD

STUDY DESIGN:

This is a prospective randomized double blinded clinical study. Both patient and observer were blinded to the group allocation. Allocations to three groups were strictly confidential and concealed. Both the patient and anesthesiologist who has injected and observed the effect of the drug were unaware of the study drugs. Those who have prepared the drug were involved in further data retrieval or analysis. Drugs of all groups were color less and look identical.

STUDY SETTING AND TIMELINES:

The study was conducted in rural based tertiary care hospital and medical college with time frame of one and half year from acceptance of synopsis.

i) Preparatory Phase-1 month
ii) Case Recruitment-6 months
iii) Data collection-12 months
iv) Data Entry&Analysis-2 month
v) Report Writing-1 month

The proposed study is to be conducted under the aegis of Department of Anaesthesia, Bankura Sammilani Medical College and Hospital, Bankura

PERIOD OF STUDY:

One and half year (18 months)

STUDY POPULATION:

Patients undergoing elective laparoscopic cholecystectomy under General Anaesthesia at General Surgery operation theatres of Bankura Sammilani Medical College and Hospital, Bankura

SAMPLE SIZE / DESIGN:

Sample Size

Based on the study of Sharma N et al [10] Patients were selected after thorough pre- anaesthetic assessment and investigations. 90 patients were divided into three groups with 30 cases in each group by

matching patient's age, sex, Mallampati score and ASA grading(I or II) and divided into three equal groups of 30 each namely group O , group P and group G,. Patients were randomly allocated in three equal groups by computer generated random number table. Allocation concealment was achieved by placing the randomization sequence for each subject in sequentially numbered sealed envelopes.

All patients were randomly allocated into 3 equal groups. (n =30)

a. Group "O": All the patients received 4mg of intravenous ondansetron just before induction of anaesthesia. This group was treated as the control group of the proposed study.
b. Group "P": All the patients received 0.075mg of intravenous palonosetron just before induction of anaesthesia.
c. Group "G": All the patients received 2mg of intravenous Granisetron just before induction of anaesthesia.

INCLUSION / EXCLUSION CRITERIA

Inclusion Criteria:

- Patients aged between 18-50 years of both the sexes.
- Patients scheduled for laparoscopic cholecystectomy under general anaesthesia.
- Patients with ASA Grade 1 or 2. (ASA Grade 1- normal healthy patient, ASA Grade 2-patient with mild systemic disease

Exclusion criteria:

- Patient refusal
- Patients who are pregnant, lactating or menstruating at the time of operation.
- Patients who received cancer chemotherapy within 4wks or emetogenic radiotherapy within 8wks before the study.
- Patients with body mass index ≥ 30.
- Patients who had experienced nausea, vomiting or taken antiemetic medication within 24hrs before surgery.
- Patients who had hypersensitivity to any of the drugs which are to be used in the study.
- Patients having co-morbid conditions like-diabetes mellitus, hypertension, airway diseases, epilepsy, endocrine diseases, ischemic heart diseases, history of allergy, liver or renal diseases, other gastrointestinal tract diseases.

STUDY VARIABLES:

- Age
- Sex
- Nausea, vomiting and retching
- Pulse rate & urine output
- Body weight
- Height
- Pain

RESULT AND DISCUSSION

This was a prospective randomized double blinded clinical study. Both patient and observer were blinded to the group allocation. Drugs of all groups were colour less and look identical All patients were randomly allocated into 3 equal groups. (n =30).

Reddy GS et al [11] (2019) found that the incidence of a complete response (no PONV and no rescue medication) during 0–3 h in the postoperative period was 90% with palonosetron; and 87.5% with palonosetron. Prophylactic therapy with palonosetron is more effective than ramosetron for long-term prevention of PONV following laparoscopic cholecystectomy.

We found that in group-G, the mean age (mean±s.d.) of patients was 34.2667 ± 8.2668 years. In group-O, the mean age (mean±s.d.) of patients was 39.0667 ± 8.8899 years. In group-P, the mean age (mean±s.d.) of patients was 38.4333 ± 8.7007 years. Distribution of mean age vs. group was not statistically significant (p=0.0699). In group-G, 18(60.0%) patients had female and 12(40.0%) patients had male. In group-O, 26(86.7%) patients had female and 14(13.3%) patients had male. In group-P, 23(76.7%) patients had female and 7(23.3%) patients had male. Association of sex vs. group was statistically significant (p=0.0572).

Distribution of mean weight and height in three groups was not statistically significant (p=0.5245& p=0.8640). Distribution of mean ASA vs. group was not statistically significant (p=0.8789).

We found that Difference of mean duration of operation and duration of anaesthesia in threee group was not statistically significant (p=0.2739 and respectively).

We found that in difference of mean SBP at different time interval in three groups was not statistically significant (p=0.7164). The mean value of SBP at 60 min was higher in group-O and it was statistically significant (p=0.0197). We found that difference of mean DBP at different time interval in three groups was not statistically significant. Difference of mean HR at different time interval in three groups was not statistically significant. The mean value of HR at 60 min was higher in group-G and it was statistically significant (p=0.0022). Difference of mean SPO2, ETCO2 at different time interval in three groups was not statistically significant.

Tahir S et al 12 (2018) found that during 24–48 h, the incidence was 17.5% and 37.5%, respectively (P = 0.04). Safety profile was similar in both the groups (P = 0.6). There were no significant differences in the overall incidence of PONV and complete responders for palonosetron and granisetron group in the early recovery period. However, due to its prolonged duration of action, palonosetron was more effective than granisetron for long-term prevention of PONV after laparoscopic. Kumar A et al 101 (2018) found that vomiting was significantly higher in group A (37.3%) as compared with group B (21.3%) at 0–48 hours (P = 0.031). Significantly more patients in Group A had nausea as compared with group B at 90–120 minutes and 6–24 hours. PCA opioid usage in microgram was significantly higher in group A at 0–24 hours and 0–48 hours.

We found that at 0 min in group-G, 30(30.0%) patients had no nausea. In group-O, 30(30.0%) patients had no nausea. In group-P, 30(30.0%) patients had no nausea. In group-G, 30(30.0%) patients had no nausea. At <2 hrs, in group-O, 22(73.3%) patients had no nausea, 3(10.0%) patients had nausea only and 5(16.7%) patients had vomiting. In group-P, 30(30.0%) patients had no nausea. Association of emesis score at <2 hrs vs. group was statistically significant (p=0.0015).

We found that in group-G, 26(86.7%) patients had no nausea and 4(13.3%) patients had nausea only. In group-O, 19(63.3%) patients had no nausea, 7(23.3%) patients had nausea only and 4(13.3%) patients had vomiting. In group-P, 27(90.0%) patients had no nausea and 3(10.0%) patients had nausea only. Association of emesis score at 2-6 hrs vs. group was statistically significant (p=0.0220).

It was found that in group-G, 28(93.3%) patients had no nausea and 2(6.7%) patients had nausea with retching. In group-O, 24(80.0%) patients had no nausea, 4(13.3%) patients had nausea only and 2(6.7%) patients had nausea with retching. In group-P, 29(96.7%) patients had no nausea and 1(3.3%) patient had nausea with retching. Association of emesis score at 6-24 hrs vs. group was not statistically significant (p=0.0632). In group-G, 26(86.7%) patients had no nausea, 1(3.3%) patient had nausea only, 1(3.3%) patient had nausea with retching and 2(6.7%) patients had vomiting. In group-O, 23(76.7%) patients had no nausea, 1(3.3%) patient had nausea only, 3(10.0%) patients had nausea with retching and 3(10.0%) patients had vomiting. In group-P, 30(100.0%) patients had no nausea. Association of emesis score at 24-48 hrs vs. group was not statistically significant (p=0.2213).

Present study found that the mean value of No. of vomiting at 2 hrs was higher in group-O and it was statistically significant (p=0.0043). The mean value of No. of vomiting 6 hrs was higher in group-O and it was statistically significant (p=0.0029). The mean value of No. of vomiting at 24 hrs was higher in group-O and it was statistically significant (p=0.0211). Difference of mean No. of vomiting at 48 hrs in three groups was not statistically significant (p=0.2745).

Tahir S et al [13] (2016) found that the frequencies of individual nausea, retching and vomiting episodes, visual analog scale (VAS) score for nausea at 2, 6, 12, 24 and 48 hours, use of rescue antiemetic (metoclopramide), number of complete responders (no PONV or use of rescue in 48 hours)

Difference of mean pain score at 0 min in three groups was not statistically significant (p=0.9831). Difference of mean pain score at 2 hr in three groups was not statistically significant (p=0.1341). Difference of mean pain score at 6 hr in three groups was not statistically significant (p=0.7109). Difference of mean pain score at 24 hr in three groups was not statistically significant (p=0.3551). The mean value of No. of vomiting at 48 hr was higher in group-G and it

was statistically significant (p=0.0201).

CONCLUSION

The effects of palonosetron, granisetron and ondansetron in preventing PONV (postoperative nausea vomiting) were compared in patients undergoing laparoscopic cholecystectomy and it was found that palonosetron was best and granisetron better in comparison with ondansetron in preventing postoperative nausea and vomiting. Palonosetron provides more effective prophylaxis of early PON (postoperative nausea), late PON (postoperative nausea), and late POV (postoperative vomiting) compared with granisetron and ondansetron. Palonosetron could provide effective prophylactic antiemetic control to prevent PONV after laparoscopic cholecystectomy surgery under general anesthesia.

Table: Distribution of mean pain score at different time of interval in three groups

		Number	Mean	SD	Minimum	Maximum	Median	p-value
Pain score at 0 min	Group-G	30	2.0667	.7849	1.0000	3.0000	2.0000	0.9831
	Group-O	30	2.0667	.7849	1.0000	3.0000	2.0000	
	Group-P	30	2.0333	.8503	1.0000	3.0000	2.0000	
Pain score at 2 hr	Group-G	30	1.9667	.8087	1.0000	3.0000	2.0000	0.1341
	Group-O	30	1.6667	.4795	1.0000	2.0000	2.0000	
	Group-P	30	1.7333	.4498	1.0000	2.0000	2.0000	
Pain score at 6 hr	Group-G	30	1.4667	.6288	1.0000	3.0000	1.0000	0.7109
	Group-O	30	1.3667	.4901	1.0000	2.0000	1.0000	
	Group-P	30	1.3667	.4901	1.0000	2.0000	1.0000	
Pain score at 24 hr	Group-G	30	.6333	.5561	0.0000	2.0000	1.0000	0.3551
	Group-O	30	.5000	.5085	0.0000	1.0000	0.5000	
	Group-P	30	.4333	.5683	0.0000	2.0000	0.0000	
Pain score at 48 hr	Group-G	30	.5000	.5085	0.0000	1.0000	0.5000	0.0201
	Group-O	30	.3000	.4661	0.0000	1.0000	0.0000	
	Group-P	30	.1667	.3790	0.0000	1.0000	0.0000	

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