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A Comparitive Study of Granisetron and Palonosetron as Antiemetics for Prevention of Post Operative Nausea and Vomiting in Patients Undergoing Laparoscopic Surgeries

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Abstract

Introduction: Laparoscopic surgeries are associated with an appreciably high rate of post operative nausea and vomiting (PONV). This study was designed to compare the effectiveness of Granisetron with that of Palonosetron for prevention of PONV after laparoscopic surgery. *Methods:* In a randomized, prospective study, 60 adult patients of both sexes received Granisetron 2.5mg and Palonosetron 75mcg intravenously at the end of surgery. Perioperative anaesthetic care was standardized in all patients. Patients were then observed 24 hours after administration of the study drug. *Results:* A complete response (defined as no PONV and no need for another rescue antiemetic) was achieved in 75% of the patients given Granisetron and 86% of the patients given Palonosetron with (P<0.05%). No significant difference observed in the recovery time from anesthesia between the two drugs and slight difference in the adverse events were observed between the two groups. *Conclusion:* This study concludes that the prophylactic intravenous administration of Palonosetron is more effective drug than Granisetron for controlling postoperative nausea and vomiting with less incidence of side effects.

Keywords: Anaesthesia; PONV; Laparoscopic Surgery; Granisetron; Palonosetron.

Introduction

The most common and distressing symptoms, which follow anesthesia and surgery, are pain and emesis. The syndrome of nausea, retching and vomiting is known as 'sickness' and each part of it can be distinguished as a separate entity. PONV (post operative nausea and vomiting) has been characterized as big 'little problem' and has been a common complication for both inpatients and outpatients undergoing virtually all types of surgical procedures.Post operative nausea and vomiting are the most unpleasant side effects after surgery. Overall incidence ranging from 18 -30% [1] or as high as 70-80% in certain high risk population without prophylaxis [2].

There are number of factors influencing the occurrence of PONV which includes patient factors (age, gender, obesity, anxiety, history of motion sickness or previous PONV and gastroparesis), operative procedures, anesthetic techniques (drugs for general anesthesia, regional anesthesia and monitored anesthesia care) and post-operative factors (pain, dizziness, ambulation, oral in-take and opoids). Laparoscopic surgery is one condition, where risk of PONV is particularly pronounced. This increased risk of PONV is due to pneumo-peritoneum causing stimulation of mechanoreceptors in the gut [2].

Anaesthetic agents initiate the vomiting reflex by stimulating the central 5-HT_3 receptors on the CTZ and also by releasing serotonin from the enterochromaffin cells of the small intestine and subsequent stimulation of 5-HT_3 receptors on vagus nerve afferent fibers.

With increasing duration of surgery and anesthesia, the risk of PONV increases possibly

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because of greater accumulation of emetogenic anesthetic agents . The incidence of PONV increases from 2.8% in patients with a surgical duration of less than 30 minutes to 27.7% in patients with a surgical duration of between151 to 180 minutes. The duration of anesthesia increases the risk for PONV by 59% for each 30-minute increase.

The consequences of PONV are physical, surgical and anesthetic complications for patients as well as financial implications for the hospitals or institutions. Physical consequences include sweating, pallor, tachycardia, and stomachache, increased chances of esophageal tear, wound dehiscence and electrolyte imbalance. Surgical consequences include disruption of vascular anastomoses and increased intracranial pressure. The anesthetic consequences are aspiration pneumonitis and discomfort in recovery. For institutions there is increased financial burden because of increased nursing care, delayed discharge from phase I and II recovery units and unexpected admissions. Hence, prophylactic antiemetic therapy is needed for all these patients. Sometimes nausea and vomiting may be more distressing especially after minor and ambulatory surgery, delaying the hospital discharge [2].

Non pharmacological techniques like acupressure, acupuncture, accustimulation, and transcutaeneous electrical nerve stimulation etc., have been given various trials but their success is limited [3].

Plenty of antiemetic drugs are available these days which include anticholinergic drugs (scopolamine, atropine), dopamine antagonist drugs (Promethazine, Prochlorperazine and Metaclopramide), antihistaminic drugs (Diphenhydramine Hydroxzine), 5HT3 receptor antagonists (Ondansetron, Granisetron, Dolasetron) and steroids (Dexamethasone). In spite of plenty of anti-emetic drugs available no single drug is 100% effective in prevention of PONV and combination therapy has got a lot of side effects [4].

Considerable progress has been made for better control of post operative nausea and vomiting in the recent years. The newer antiemetics like 5 – Hydroxytryptamine 3 receptor (5HT3) antagonists are potent therapeutic agents with fewer side effects.

Granisetron is one of the more selective 5HT 3 receptor antagonist which has a elimination half life of 9 hours It has lesser side effects unlike the contemporary antiemetics [4]. Palonosetron is the most recent 5HT3 receptor antagonist first introduced for management of chemotherapy induced nausea and vomiting. Its half life is about 40 hours [5]. Laparoscopic surgeries are the preferred surgical procedure these days. It has considerably decreased the surgical mortality but the incidence of post operative nausea and vomiting remains high and hence prophylactic antiemetics are indicated [6].

Patients receiving general anesthesia were 11 times more likely to experience PONV than those who received monitored anesthesia care, regional anesthesia or chronic pain block.

The present study was undertaken to compare the antiemetic effects of IVGranisetron and Palonosetron for prophylaxis of postoperative nausea and vomiting in patients undergoing laparoscopic surgery.

Methodology

In this study, 60 patients in the age group of 20-50yrs, belonging to ASA grade I & II Scheduled for elective laparoscopic surgery under GA were included.

Patients were randomly divided into two groups of 30 each.

Group 'G' –GRANISETRON group(n = 30)

Group 'P' –PALONOSETRON group (n = 30)

Pre-Anesthetic Assessment

On the day prior to surgery a thorough clinical examination of the patient was performed including General Physical Examination & systemic examination (Cardiovascular system, Respiratory system, Central nervous system, Gastro-intestinal system), H/O Drug allergy, Airway assessment was done by Mallampatti Grading.

All patients were explained about the anesthesia technique & written informed consent was taken.

Patients were kept NPO for 8hrs prior to surgery.

Lab Investigation

Routine investigation were done. (Hb%, Blood grouping, BT, CT, DC, Urine analysis, Serum creatinine, Fasting blood sugar, ECG) No specific investigations required pertaining to the study.

Pre-Medication

All patients were given tablet diazepam 5mg orally at bed time on the previous night of surgery to alley anxiety and apprehension.

Technique of Anaesthesia

60 patients aged between 20-50 yrs of either sex belonging to ASA grade I & II were randomly divided into 2 groups , each group consisted of 30 patients.

Group G (Granisetron group)

Group P (Palonosetron group)

Anesthesia machine, circuits checked, resuscitation equipments were kept ready.

On the day of surgery after confirmation of NPO status patients were shifted to operating room and routine monitoring devices pulse oximetry, NIBP, ECG monitors were attached, and baseline blood pressure, heart rate, ECG and O_2 saturation values were recorded. Later capnography was attached after the intubation.

Continuous monitoring of the vital parameters were done.

An IV line was secured with an appropriate sized cannula in all patients and IV fluids were started. Prior to induction, injection Glycopyrolate 0.2mg administered IV, Inj Fentanyl 1.5 μg/kg IV.

All patients were pre oxygenated for 3 min and anesthesia was induced with Thiopentone sodium (5mg/kg), after successful trial ventilation, vecuronium 0.1mg/kg given to facilitate laryngoscopy and intubation. Oxygenation was continued by positive pressure mask ventilation using Bains circuit. After 3 mins using laryngoscope Macintosh blade intubation was done with well lubricated, appropriate sized cuffed oral endotracheal tube. After confirmation of the tube position cuff was inflated, tube fixed, connected to Boyle's machine through Bains circuit. Anaesthesia was maintained with N_2O, O_2, isoflurane, controlled ventilation with appropriate fresh gas flow to maintain blood pressure and heart rate within 20% of preinduction values. Capnography was connected and patients were mechanically ventilated to keep $EtCO_2$ between 35-40 mm Hg.

Surgery was allowed to commence. During surgery the patients were placed in trendlenburg position whenever required and positions of the patients was changed based on surgical requirement. A nasogastric tube was inserted to make the stomach empty of air and other contents, peritoneal cavity was insufflated with carbon dioxide to keep intra abdominal pressure <12mmHg. Anaesthesia was continued with N_2O (50%), O_2(50%),isoflurane. Vecuronium top up doses, analgesics (Fentanyl 1.5mcg/kg) and IV fluids administered based on the requirements.

Patients received one of the study drugs at the end of surgery, Group I (Granisetron group) patients received IV granisetron 2.5 mg in 2.5 ml & Group II (palonosetrongroup) patients received IV palonosetron 75μg in 2.5 ml administered slow iv over period of 30 seconds.

At the completion of surgery patients were made supine , when they had respiratory attempts residual neuromuscular block was reversed with injglycopyrollate 10 μg/kg and neostigmine 0.05mg/kg Before tracheal extubation, the nasogastric tube was suctioned and removed, Recovery was assessed with Recovery time &extubation was done after thorough throat suction.

Recovery Time (RT)

Recovery time in minutes was measured from the time Nitrous Oxide is switched off until the patient respond to simple verbal commands.

After complete clinical recovery patients were shifted to post anesthesia care unit.

The patients then were assessed with the help of clinical recovery score.

Clinical Recovery Score (CRS)

The clinical recovery score was assessed at 0, 1, 2, 3 and 4 hours after patient's arrival in recovery room and assessments was done and appropriate recording were taken The score consisted of simple questions to evaluate vigilance, cognition and orientation.

Results

Table 1: Weight Distribution

Weight Range (in KGS)	Granisetron	Palonosetron
45-60	20 (67%)	23 (77%)
61-70	10 (33%)	7(23%)
Mean weight ±SD	56.93±10.62	50.86±10.85

There was no significant weight difference between the two groups

Table 2: Asa grade wise

Grade	Granisetron	Palonosetron
I	25 (83%)	23 (77%)
II	5 (17%)	7 (23%)

Both groups had almost similar numbers of ASAI and ASAII

Table 3: Surgical procedures done

Surgical Procedure	Granisetron	Palonosetron
Laproscopic tubal occulusion (LTO)	18 (60%)	15 (50%)
LaproscopicAppendicectomy (LAPP)	2 (7%)	6 (20%)
Laproscopic Cholecystectomy (LCHO)	7 (23%)	5 (17%)
Diagnostic Laproscopy	3 (10%)	3 (10 %)
LaproscopicHernioplasty	0 (0%)	1 (3%)

The above types of procedure were included in our study. LTO predominated in both groups than any other surgeries

Table 4: Incidence of nausea

Duration	Granisetron (n=30)	Palonosetron (n=30)
0-4hr	**4 (14%)	**2 (7%)
4-12hr	*2(7%)	*1 (4%)
12-24hr	1(4%)	0 (0%)

Occurrence of nausea in granisetron group and Palonosetron group showed that incidence of nausea in 0-4 hours were 4 cases (14%)in Granisetron group as compared to 2 cases (7%) in Palonosetron group (P<0.01).

Incidence of nausea in 4-12 hours were 2 cases (7%)in Granisetron group as compared to 1 cases (4%) in Palonosetron group (P<0.05).

Incidence of nausea in 12-24 hours was only 1 case (4%) in Granisetron group as compared to 0 cases (0%) in Palonosetron group. The incidence of nausea was maximum during the first four hours and it was more in the Granisetron group.

Incidence of vomiting episodes in granisetron group were 4 cases (14%) as compared to 2 cases (7%) in palonosetron group in 0-4 hours (P<0.01).

In 4-12 hours granisetron group had 3 cases (10%) of incidence of vomiting as compared to 1 case (4%) in palonosetron group (P<0.05). Again the incidence of vomiting was maximum during first four hours and no patient in any group vomited from 12 hours onwards.

Table 5: Incidence of vomiting

Duration	Granisetron (n =30)	Palonosetron (n=30)
0-4hr	**4 (14%)	**2 (7%)
4-12hr	*3 (10%)	*1 (4%)
12-24hr	0 (0%)	0

Table 6: Comparison of rescue antiemetic

Anesthetic Sequlae	Granisetron (n=30)	Palonosetron (n=30)
Rescue antimetic	7 (23 %)	3 (10 %)

Need for rescue antiemetic is more in Granisetron group compared to palonosetron group.

Discussion

Postoperative nausea and vomiting (PONV) is of multifactorial origin. The incidence of PONV after anaesthesia, despite the advances in antiemetic therapy in the last decades is still found to be relatively high. Gold et al noted that the three most common causes for admission following day care surgery are pain, bleeding and intractable vomiting [7].

Factors affecting PONV include patient related factors (age, sex, phase of the menstrual cycle), anaesthesia related factors (use of volatile anesthetic agents, N_2O, Opioid) and surgery related factors [7]. Female gender has been associated with higher

incidence of PONV compared to male patients [7,8]. On an average, female patients suffer three times more often from PONV than men.

Our study was aimed at comparing the antiemetic efficacy of Granisetron and Palonosetron in preventing PONV in laparoscopic surgery. In our study the factors that would have contributed to nausea and vomiting may be laparoscopic surgery, use of Halothane, use of Fentanyl etc. Use of facemask, use of Nitrous Oxide may or may not have contributed to nausea and vomiting. Laparoscopic surgery was chosen because of high incidence of PONV associated with it. Naguib et al demonstrated that the incidence of PONV after laparoscopic surgeries in their placebo group was remarkably high (72%) [9]. We have conducted studies on 60 patients of ASA I and II with demographic data in terms of age, weight, which were similar in the two groups. There was no significant difference in Granisetron and Palonosetron ($P < 0.05$) in terms of Age and Weight.

Study done by Pearman [8] shows that postoperative nausea and vomiting is more common in young age group and obese patients.

Incidence of nausea in our study group was 25% in Granisetron group, 11% in Palonosetron group. Present study shows highly significant difference in first 0-4hr ($P < 0.05$). While in 4-12hrs incidence of nausea shows marginally significant difference. After 12-24hrs, there was no significant difference in nauseating episodes. Study done by Pueyo [10] observed that nausea and vomiting is more common in first 6 hours post operatively. Same results are seen in the study done by Fujii [11]. Vomiting in the present study group was 24% in Granisetron, 11% in the Palonosetron group. In our study group incidence of vomiting was highly significant in first 4hrs ($P<0.01$). Present study showed that Palonosetron is better than Granisetron for preventing PONV. Bhattacharjee [5] in his study observed same results. The incidence of a complete response (no PONV, no rescue medication) during 0-3 hour in the postoperative period was 86.6% with granisetron and 90% with palonosetron, the incidence during 3-24 hour postoperatively was 83.3% with granisetron and 90% with palonosetron. During 24-48 hour, the incidence was 66.6% and 90% respectively ($p<0.05$). The incidence of adverse effects were statistically insignificant between the groups. Janknegt [12] studied that if Ondansetron is given at the induction time, it is ineffective in preventing PONV, So we administered study drug half an hour before end of the surgery. This makes the drugs to be effective postoperatively for longer time. Sinha [53] concluded the same results in his study.

Conclusion

- Nausea and vomiting is more common in female patients undergoing laparoscopic surgery.
- Palonosetron is more effective than Granisetronin preventing postoperative nausea and vomiting.
- Palonosetron has fewer incidences of side effects as compared to Granisetron.
- Use of rescue antiemetic is less with the Palonosetron as compared to Granisetron.
- Palonosetron is more potent and longer acting as compared to Granisetron.

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