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Comparison of granisetron and palonosetron for the prevention of postoperative nausea and vomiting in patients undergoing laparoscopic surgery: a prospective randomised study.

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ABSTRACT

INTRODUCTION: Postoperative nausea and vomiting (PONV), a common and uncomfortable consequence of anaesthesia and surgery, can lead to dehydration, alkalosis, aspiration, and psychological distress, including a reluctance to undergo future surgical procedures. The aim of the study was to compare the effect of Granisetron and Palonosetron on the prevention of postoperative nausea and vomiting in patients undergoing laparoscopic surgery under general anaesthesia.

MATERIALS AND METHODS: In this randomised prospective study, after a full preoperative evaluation and investigation, patients meeting the inclusion criteria were taken for the study. 80 patients were selected and randomly divided into two groups. Group G received 40 mcg/kg of granisetron and group P was administered palonosetron 1 mcg/kg before induction of anesthesia. The patients were monitored in the postoperative period and PONV scores were observed at 0-2, 4-6, 6-12, and 12-24 hours postoperatively. Rescue antiemetic, in the form of Dexamethasone 4 mg IV, was administered with PONV score <1.

RESULTS: There were no statistically significant differences between the two groups with respect to the classification of ASA, the sex distribution, age, BMI or the duration of anaesthesia, making the two groups comparable. PONV scores were comparable between the two groups during 0 to 2 hours and 2 to 6 hours postoperatively (p value>0.05). During the 6- to 12-hour interval and the 12- to 24-hour interval, PONV scores were significantly lower in patients in Group P (p-value 0.022). There was no statistically significant difference between the antiemetic rescue requirement between the group G and group P (p-value 0.152).

CONCLUSIONS: This study concludes that both granisetron and palonosetron are effective in controlling PONV in the immediate postoperative period, but palonosetron is superior to granisetron in preventing PONV beyond 6 hours.

KEY WORDS: Granisetron, palonosetron, PONV, laparoscopic surgery, nausea, vomiting.

INTRODUCTION

Postoperative nausea and vomiting (PONV) a common and distressing consequence of anaesthesia and surgery, carrying various adverse effects such as dehydration, electrolyte imbalance, risk of aspiration, and psychological implications such as surgery aversion [1,2]. Severe retching and vomiting can lead to some rare but grave complications such as wound dehiscence, bleeding, esophageal rupture, subcutaneous emphysema, pulmonary aspiration, and bilateral pneumothorax. PONV also has cost implications in terms of increased nursing time, delayed recovery, increased utilisation of hospital resources, delayed discharge, and possible reoperation costs [3].

There are many factors that determine the risk of PONV. Characteristics of age, female gender, history of motion sickness, obesity, anxiety, etc. lead to an increase in the incidence of PONV [4]. The causes related causes of PONV include the use of nitrous oxide, volatile anaesthetics, and postoperative opioids [5]. In addition, certain types of surgery are also associated with a higher incidence of PONV. These include upper abdominal surgery, laparoscopic surgery, surgery of middle ear surgery, and head & neck surgery [6,7]. Laparoscopic surgery is the second most common cause of PONV, with an incidence ranging from 46-82%. The principal reason behind this is the creation of the carbon dioxide pneumoperitoneum which causes diaphragmatic stimulation and stretching of peritoneal mechanoreceptors, leading to increased serotonin synthesis, leading to PONV.

The 5-hydroxytryptamine 3 (5-HT3) receptors, which are located at the vagus nerve terminal in the periphery and on chemoreceptor trigger zone (CTZ) of the area post-rema, are the principal receptors responsible for PONV. Therefore, 5-HT3 receptors antagonists are currently the most popular class of drugs used for the prevention of PONV. Ondansetron, a first-generation 5-HT3 receptor antagonist, is one of the most commonly used drugs for this purpose. Apart from Ondansetron, Granisetron, another first generation 5-HT3 receptor antagonist, and Palonosetron, a second generation 5-HT3 receptor antagonist, have become quite popular over the years. However, there are conflicting reports on the comparative evaluation of both these drugs [8-11]. Therefore, the aim of the study was to compare the effect of Granisetron and Palonosetron on the prevention of postoperative nausea and vomiting in patients undergoing laparoscopic surgery under general anaesthesia.

MATERIALS AND METHODS

This prospective randomised study was conducted after approval from the institutional ethical committee [TP(MD/MS) (43/2020)/IEC/ABVIMS/RMLH/330] and registration with the clinical trial registry of India (CTRI/2021/09/045852). The calculation of the sample size was based on a study conducted by Lele S, et al. [1], it was found that the incidence of PONV in the granisetron group was 3.30% and in the palonosetron group was 6.70%. β risk of 90% at an α level of 0.05 to detect a reduction of 20% in the incidence of PONV for patients in the study groups. 38.46 patients per group were sufficient to detect a significant difference. So, for the total sample size we have taken 80 patients.

Consequently, eighty American Society of Anesthesiologists (ASA) grade I and II patients, in the age group of 18-65 years, undergoing elective laparoscopic surgery under general anaesthesia were included in the study. Exclusion criteria included patients with renal or liver dysfunction, those on serotonin reuptake inhibitors, a history of motion sickness or PONV, a known allergy to the study drug, a history of opioid abuse, those receiving chemo or radiation therapy, and pregnant females.

Written and informed consent was given by all the patients. After a comprehensive preoperative evaluation and investigation, patients who met the inclusion criteria were selected for the study. The selected patients were randomly divided into 2 groups of 40 patients each using computer generated randomisation. Group G received Granisetron 40 mcg/kg intra venous (IV), while group P received Palonosetron 1 mcg/kg IV. After shifting the patient to the operating table, standard monitoring in the form of electrocardiogram, heart rate, noninvasive blood pressure, Pulse oximetry were attached. Baseline vitals were recorded. A wide-bore intravenous cannula was secured and IV fluid infusion was started. Patients in group G received Granisetron 40 mcg/kg IV and patients in group P received Palonosetron 1 mcg/kg IV prior to induction of anesthesia. General anaesthesia was induced using midazolam 0.02 mg/kg, fentanyl 2 mcg/kg and propofol 2mg/kg. Vecuronium bromide (0.1mg/kg) was used to facilitate laryngoscopy and tracheal intubation. Laryngoscopy and intubation were performed after 3 minutes of Vecuronium bromide administration using cuffed endotracheal tube. Anaesthesia was maintained with sevoflurane and oxygen – air mixture (50:50), and ventilation was adjusted to maintain end-tidal carbon dioxide (EtCO2) of 30-35 mm of Hg throughout the procedure. The pneumoperitoneum was created using the Veress needle technique and intraabdominal pressure was maintained at 12 to 14 mm of Hg. For postoperative analgesia, 15 mg/kg IV paracetamol infusion and surgical ports were infiltrated with 0.25% bupivacaine. Reversal of neuromuscular blockade was achieved with neostigmine (0.05 mg/kg IV) and glycopyrrolate (0.01 mg/kg IV) at the end of surgery. After returning protective airway reflexes, trachea was extubated.

After completion of the procedure, the patients were transferred to the post-anaesthesia care unit and PONV was monitored using PONV score at 0-2, 2-6, 6-12 and 12-24 hours postoperatively. In case of no nausea, vomiting, or vomiting, the PONV score was found to be zero. Nausea without retching or vomiting was assigned a PONV score of one. The vomiting was assigned a PONV score of two, while vomiting was assigned a score of three. Rescue antiemetic, in the form of Dexamethasone 4 mg IV, was administered with PONV score <1.The primary objective of this study was to compare the effect of Granisetron and Palonosetron on the prevention of postoperative nausea and vomiting the first 24 hours after laparoscopic surgery performed under general anaesthesia. The secondary objective of this study was to compare the antiemetic rescue requirement between group G and group P.

In statistical analysis was performed using the SPSS programme for Windows, version 21.0. Continuous variables are presented as mean ± SD, and categorical variables are presented as absolute numbers and percentage. The data was checked for normality prior to statistical analysis.

Normally distributed continuous variables were compared using the unpaired t-test, whereas the Mann-Whitney U test was used for those variables that were not normally distributed. Categorical variables were analysed using the chi-square test or Fisher's exact test. For all statistical tests, a p-value less than 0.05 was taken to indicate a significant.

RESULTS

During the study, 87 patients were assessed for eligibility. Seven of them did not meet the inclusion criteria and were excluded. The remaining eighty patients were randomised into two groups of 40 patients each (Figure 1).

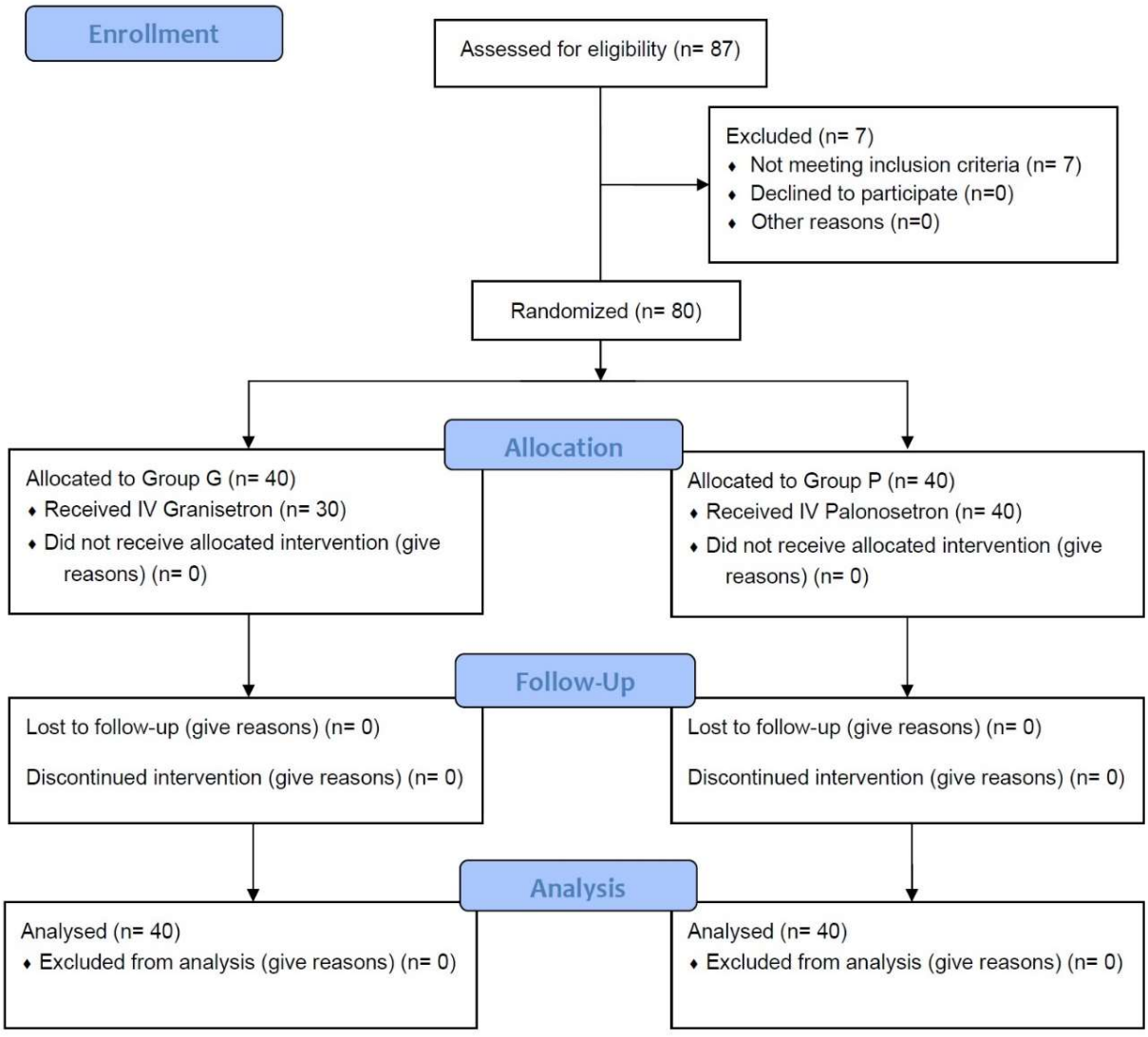

Figure 1. Consort flow diagram.

No significant differences in age (years) between group G (Mean ± SD 36.77 ± 12.55) and group P (Mean ± SD 39.25 ± 11.98) (p-value = 0.150). No significant differences were observed in BMI (Kg m^{-2}) between group G (Mean ± SD 21.60 ± 2.51) and group P (Mean ± SD 22.19 ± 1.48) (p-value = 0.099). No significant differences were observed in the duration of anaesthesia (minutes) between group G (Mean ± SD 117.50± 7.76) and group P (Mean ± SD 115.88 ± 8.76) (p-value = 0.460). There was no statistically significant difference between group G and group P with respect to the classification of ASA and sex distribution (Table 1).

Table 1. Comparison of baseline characteristics between the G group and the P group.

Variable	Group G (n = 40)		Group P (n = 40)		P value
	Mean (SD)	Median (IQR)	Mean (SD)	Median (IQR)	
Age (Years)	36.77 (12.55)	32.5 (27.75 - 41.25)	39.25 (11.98)	36.5 (32 – 46)	0.150
BMI (Kg m^{-2})	21.60 (2.51)	21.2 (19.5 - 23.5)	22.19 (1.48)	22.5 (20.8 - 23.5)	0.099
Duration of Anesthesia (minutes)	117.50 (7.76)	120 (110 - 120)	115.88 (8.76)	120 (110 - 120)	0.460
ASA Class	(n = 40)	**%**	(n = 40)	**%**	
Class I	34	85.0	34	85.0	1.000
Class II	6	15.0	6	15.0	
Sex	(n = 40)	%	(n = 40)	%	
Female	20	50.0	23	57.5	0.501
Male	20	50.0	17	42.5	

SD: Standard deviation, IQR: Interquartile range, BMI: Body mass index, ASA: American Society of Anesthesiologists

Table 2. Comparison of the PONV score at 0-2 hours between the G group and the P group.

PONV Scoring (0-2 Hours)	Group			Fisher's Exact Test	
	G (n = 40)	P (n = 40)	Total	χ2	P Value
Score 0	34 (85.0%)	31 (77.5%)	65 (81.2%)		
Score 1	2 (5.0%)	4 (10.0%)	6 (7.5%)		
Score 2	3 (7.5%)	2 (5.0%)	5 (6.2%)	2.005	0.617
Score 3	1 (2.5%)	3 (7.5%)	4 (5.0%)		
Total	40 (100.0%)	40 (100.0%)	80 (100.0%)		
PONV Score (0-2 Hours)	**Group**			**Wilcoxon-Mann-Whitney U Test**	
	G		P	W	p value
Mean (SD)	0.28 (0.72)		0.42 (0.90)		
Median (IQR)	0 (0-0)		0 (0-0)	739.500	0.396
Range	0 – 3		0 - 3		

Table 3. Comparison of the PONV score at 2-6 hours between the G group and the P group.

PONV Scoring (2-6 Hours)	Group			Fisher's Exact Test	
	G (n = 40)	P (n = 40)	Total	χ2	P Value
Score 0	39 (97.5%)	40 (100.0%)	79 (98.8%)		
Score 1	0 (0.0%)	0 (0.0%)	0 (0.0%)		
Score 2	1 (2.5%)	0 (0.0%)	1 (1.2%)	1.013	1.000
Score 3	0 (0.0%)	0 (0.0%)	0 (0.0%)		
Total	40 (100.0%)	40 (100.0%)	80 (100.0%)		
PONV Score (2-6 Hours)	**Group**			**Wilcoxon-Mann-Whitney U Test**	
	G		P	W	p value
Mean (SD)	0.05 (0.32)		0.00 (0.00)		
Median (IQR)	0 (0-0)		0 (0-0)	820.000	0.330
Range	0 – 2		0 - 0		

Table 4. Comparison of the PONV score at 6-12 hours between the G group and the P group.

PONV Score (6-12 Hours)	Group			Fisher's Exact Test	
	G (n = 40)	P (n = 40)	Total	χ2	P Value
Score 0	35 (87.5%)	40 (100.0%)	75 (93.8%)		
Score 1	0 (0.0%)	0 (0.0%)	0 (0.0%)		
Score 2	1 (2.5%)	0 (0.0%)	1 (1.2%)	5.333	0.055
Score 3	4 (10.0%)	0 (0.0%)	4 (5.0%)		
Total	40 (100.0%)	40 (100.0%)	80 (100.0%)		

PONV Score (6-12 Hours)	Group		Wilcoxon-Mann-Whitney U Test	
	G	P	W	p value
Mean (SD)	0.35 (0.95)	0.00 (0.00)		
Median (IQR)	0 (0-0)	0 (0-0)	900.000	0.022
Range	0 – 3	0 - 0		

Table 5. Comparison of the PONV score at 12-24 hours between the G group and the P group.

PONV Scoring (12-24 Hours)	Group			Fisher's Exact Test	
	G (n = 40)	P (n = 40)	Total	χ2	P Value
Score 0	35 (87.5%)	40 (100.0%)	75 (93.8%)		
Score 1	2 (5.0%)	0 (0.0%)	2 (2.5%)		
Score 2	1 (2.5%)	0 (0.0%)	0 (1.2%)	5.333	0.055
Score 3	2 (5.0%)	0 (0.0%)	2 (2.5%)		
Total	40 (100.0%)	40 (100.0%)	80 (100.0%)		

PONV Score (12-24 Hours)	Group		Wilcoxon-Mann-Whitney U Test	
	G	P	W	p value
Mean (SD)	0.35 (0.95)	0.00 (0.00)		
Median (IQR)	0 (0-0)	0 (0-0)	900	0.022
Range	0 – 3	0 - 0		

The mean PONV score at 0-2 hours in group G was 0.28 ± 0.72 and group P was 0.42 ± 0.90. No significant differences between the groups. (p=0.396). The mean PONV score at 2-6 hours in group G was 0.05 ± 0.32 and group P was 0.00 ± 0.00. No significant difference between the groups. (p=0.330). The mean PONV score at 6-12 hours in group G was 0.35 ± 0.95 and group P was 0.00 ± 0.00. The significant difference between the groups (p=0.022). The mean PONV score at 12-24 hours in group G was 0.35 ± 0.95 and group P was 0.00 ± 0.00. The significant difference between the groups (p=0.022). PONV scores were comparable in both groups up to 6 hours, but were significantly lower in group P between 6-12 hours and 12-24 hours postoperatively (Tables 2-5). The rescue antiemetic was 40% in group G patients and 25% in group P patients. The requirement of rescue antiemetic was comparable between group G and group P (p=0.152) (Table 6).

Table 6. Requirement of rescue antiemetic used between the G group and the P group.

Rescue Antiemetic Used	Group			Chi-Squared Test	
	G (n = 40)	P (n = 40)	Total	χ2	P Value
Yes	16 (40.0%)	10 (25.0%)	26 (32.5%)		
No	24 (60.0%)	30 (75.0%)	54 (67.5%)	2.051	0.152
Total	40 (100.0%)	40 (100.0%)	80 (100.0%)		

DISCUSSION

PONV continues to be a major burden for patients undergoing surgery. Although it is rarely life-threatening, it has a significant effect on the patient's well-being and is often listed as one of surgery and anesthesia's unfavourable side effects [12]. PONV increases perioperative morbidity, prolongs hospital stay, leads to readmissions and increases overall financial burden [13].

In this study, the effects of Granisetron (40 mcg Kg-1 IV) and Palonosetron (1 mcg Kg-1) on PONV in patients undergoing laparoscopic surgery. In this study, granisetron and palonosetron were found to be effective in preventing PONV and the effects of both the drugs was comparable up to 6 hours postoperatively. Between the 6-12 hours interval and 12-24 hours, palonosetron was found to be significantly more effective. This may be attributed to the fact that palonosetron has a longer half-life compared to granisetron (40 hours vs. 9 hours), leading to its better performance beyond 6 hours. Hatti et al. [11] conducted a study and reported that the incidence of PONV was significantly lower in the palonosetron group compared to granisetron group in postoperative intervals of 0-4 hours (7% vs. 14%, $p < 0.01$) and 4-12 hours (4% vs. 10%, $p < 0.05$) intervals. None of the patients in either group reported PONV at an interval of 12-24 hours. These results are in agreement with this study.

A statistically significant difference between the two groups during the 0-4 hour interval may be because of the difference in the doses of palonosetron (75 mcg) and granisetron (2.5 mg) administered, compared to our study. Kathuria et al. [14] conducted a study on 135 patients and randomly divided them into 3 groups of 45 patients each. Group P received palonosetron (0.075 mg), group O received ondansetron (8 mg) and group G was administered granisetron (2.5 mg). The authors reported a significantly lower incidence of PONV in the palonosetron group (4.4%), compared to the ondansetron (20%) and granisetron (26.7%) groups. These results are again similar to those received in the current study. Manohar et al. [15] compared the effect of palonosetron and granisetron on PONV in 100 patients. They reported a comparable incidence of PONV in both groups during the first 2 hours postoperatively. However, the incidence of PONV in the palonosetron group was significantly lower than in the granisetron group during the 2 to 24 hours interval. These results are quite similar to those received in the present study.

The major limitation of our study is that we compared granisetron and palonosetron in their optimal doses and not in equipotent doses. The study was carried out in ASA, of grade 1 and 2 adult patients so extrapolation of the study results of study on geriatric and paediatric patients.

CONCLUSIONS

In conclusion, our study demonstrates that both palonosetron and granisetron are equally effective in controlling PONV in the immediate postoperative period, but palonosetron was superior to granisetron for PONV prophylaxis beyond 6 hours.

SUPPLEMENTARY INFORMATION

Funding: *No fund was received related to this study.*
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Informed Consent Statement: *Not applicable*
Data Availability Statement: *The datasets generated and analyzed during the current study are available from the corresponding author on reasonable request.*
Conflicts of Interest: *The authors declare no conflicts of interest.*
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