

Comparison of ondansetron HCl, granisetron HCl and palonosetron HCl for prevention of postoperative nausea and vomiting following gynaecological surgery under general anaesthesia

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Abstract

Context: Postoperative Nausea and Vomiting (PONV) is associated with many adverse events, which prolong and increase the healthcare cost.

Aims: To compare the efficacy of Palonosetron with respect to Granisetron and Ondansetron in prevention of PONV. To study the need of rescue antiemetic and incidence of side effects.

Settings and Design: This Prospective, Randomized study was carried out with 150 adult female patients of ASA Grade I & II posted for elective gynecological surgery under GA.

Materials and Methods: Patients were divided into three groups of 50 patients each.

Group O received injection ondansetron 8 mg IV, Group G received Granisetron 2.5 mg IV & Group P received Palonosetron 0.075 mg iv before GA induction.

Episodes of nausea, vomiting, need for rescue antiemetic and side effects were observed for 72 hours in postoperative period.

Statistical Analysis Used: Graphpad Software with consideration of significant *P* value <0.05.

Results: Incidence of nausea and vomiting was more with Ondansetron and minimal with Palonosetron with statistical significance of *P*< 0.05.

Lowest incidence of nausea was found with Palonosetron during 3-24 hours postoperatively (*P*<0.0068)

Complete Control of PONV (No PONV, No rescue drug required) was maximum in P group in all hours of study [*P*<0.05]. Inj Ondansetron 8 mg IV was used as rescue drug. No difference in side effect was observed.

Conclusion: Palonosetron is safe, well tolerated and effective than Granisetron and Ondansetron in reducing the incidence of PONV with less need of rescue antiemetics.

Key Messages: Palonosetron is proved better antiemetic than granisetron and ondansetron in prevention of PONV.

Keywords: General Anaesthesia, Granisetron, Gynaecological surgery, Ondansetron, Palonosetron, Postoperative nausea and vomiting.

Introduction

Postoperative nausea and vomiting (PONV) is episodes of nausea or vomiting occurring upto 24 hours post surgery. Incidence of PONV is 75-80% in high-risk category.¹ Incidence of PONV after gynaecological surgeries is 58%-75%.²

5HT₃ receptor antagonists are effective antiemetics with favourable drug profile. This study was done to compare these three antiemetics in terms of efficacy and side effects. Ondansetron is the first drug to be used for prophylaxis due to its lower cost. Granisetron is selective and produces irreversible blockade. Palonosetron belongs to the second-generation with unique chemical structure; it binds in an allosteric manner such that serotonin binding is indirectly inhibited.³⁻⁷

Materials and Methods

After attainment of ethical committee approval and written consent from all patients this Prospective, Randomised study was conducted in 150 female patients undergoing gynaecological surgeries.

Patients were randomly divided into three groups each containing 50 patients.

Inclusion Criteria: Patients included were ASA grade I & II female patients of age between 25 to 65 years undergoing elective gynaecological Surgeries

Exclusion Criteria:

1. History of gastro-oesophageal reflux.
2. Scheduled to undergo emergency surgery or minor surgery not requiring laparotomy.
3. Usage of propofol during maintenance phase of anaesthesia.
4. Usage of drug with potential anti emetic effect within 24 hrs prior to the administration of anaesthesia.
5. History of allergic reactions to antiemetics.
6. Patient with vomiting from any organic cause; vomiting or nausea in 24 hrs preceding the administration of anaesthesia.

Patients were assessed at preoperative visit.

Patients were "nil by mouth" after 10 pm on the previous night before operation.

Premedication with Tab Lorazepam 1 mg was given at 10 pm on previous night.

After taking patient in OT, IV line was established. Essential Monitors in the form of ECG, SpO₂, NIBP were applied, and parameters were observed.

Premedication in the form of Inj. Glycopyrrolate (0.004 mg/kg). Epidural catheter was inserted in L1-L2 or L2-L3 space for postoperative analgesia.

Ondansetron, Granisetron and Palonosetron were given to respective group of patients just before induction of general anaesthesia.

Group O: IV Inj. ondansetron hydrochloride 8 mg.

Group G: IV Inj. granisetron hydrochloride 2.5 mg.

Group P: IV Inj. palonosetron hydrochloride 0.075 mg.

After preoxygenation with 100% O₂, induction, Inj. Fentanyl citrate (2µg/kg) IV, Inj. Thiopentone Sodium (5-6 mg/kg) IV and Inj. Succinylcholine hydrochloride (2mg/kg) IV.

After which patients were intubated with suitable size oral portex cuffed endotracheal tube and Nasogastric tube was inserted.

Maintenance was done with 50 % O₂ + 50 % N₂O + Isoflurane. Inj. Vecuronium Bromide (0.08 mg/kg) IV was used as non-depolarizing muscle relaxant.

Intraoperative monitoring was done throughout surgery.

All patients reversal done with Inj. Glycopyrrolate (0.008 mg/kg) and Inj. Neostigmine (0.05mg/kg) IV.

Patients were assessed for episodes of nausea, vomiting and need of rescue antiemetic and side effects up to 72 hrs post-operative period.

Inj. Ondansetron HCl 8 mg IV was given as "RESCUE" antiemetic for persistent nausea or vomiting.

Statistical Analysis

Results were analysed by one way ANOVA test and chi square test for demographic data comparison. The results were defined as significant if P value was < 0.05. All these statistical analyses were performed using Graph pad software.

Table 1: Demographic data

	Group O	Group G	Group P	P value
Age(years)	45.74± 9.6	47.88 ±9.5	46.4±9.5	0.52
Weight (kg)	57.26±7.5	57.46±7.4	57.9±8.2	0.91
ASA Status (I/II)	34/16	37/13	36/14	0.79
Duration of Surgery	207.5±41.6	209.4±45.6	207.7±42.6	0.97

Table 2: Type of surgeries

	Group O n=50	Group G n=50	Group P n=50
Radical hysterectomy	8	9	12
TAH+BSO	13	17	17
TAH+USO	6	1	3
Staging laparotomy	6	8	7
Interval laparotomy	4	5	3
Exploratory laparotomy	13	10	8

Results

Demographic data of the study is specified in Table 1.

Types of surgeries considered in study are notified in Table 2.

All three groups were comparable in respect to the type of surgeries.

Incidence of Nausea in three study groups mentioned in Table 3.

Incidence of nausea was relatively high in ondansetron group as opposed to Granisetron and Palonosetron group in all time intervals. Least episodes in Palonosetron group was significant as $P < 0.05$; highly significant in 3 to 24 hrs period as $P < 0.01$, as displayed in Graph 1.

Incidence of Vomiting in three study groups mentioned in Table 4.

Same as for nausea, the incidence of vomiting was highest in Ondansetron group and least in Palonosetron group. The difference was significant in all time intervals as $P < 0.05$, as shown in Graph 2.

Requirement of rescue antiemetic was least in Palonosetron group.

The difference between three groups was significant as < 0.05 , as shown in Graph 3.

When three groups were compared for complete response, the difference was significant as $P < 0.05$. Incidence of complete response was highest in Palonosetron group and lowest in Ondansetron group during all time intervals, as shown in Graph 4.

While comparing incidence of side effects like headache, dizziness and drowsiness between these groups, it was less in Granisetron and Palanosetron group, but the difference was insignificant as $P > 0.05$.

No treatment was required for these side effects and they gradually resolved on their own mostly after 24 to 48 hrs.

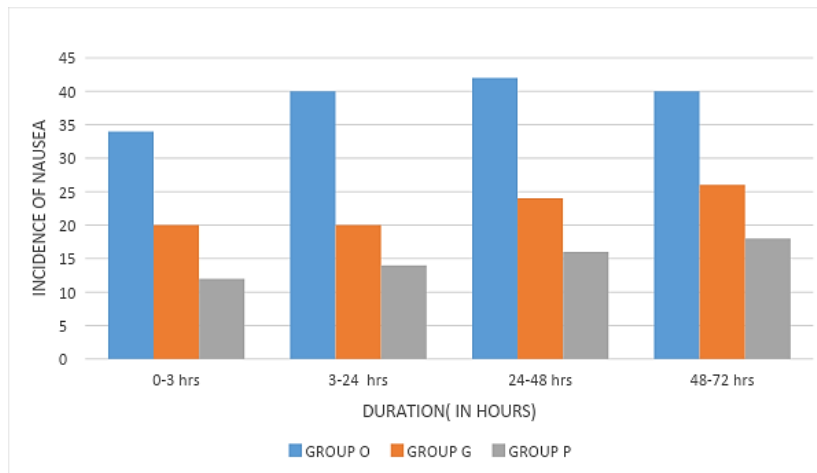
Table 3: Incidence of nausea in three study groups

	Group O n (%)	Group G n (%)	Group P n (%)	P value
0-3 hrs	17(34)	10(20)	6(12)	0.027
3-24 hrs	20(40)	10(20)	7(14)	0.006
24-48 hrs	21(42)	12(24)	8(16)	0.012
48-72 hrs	20(40)	13(26)	9(18)	0.046

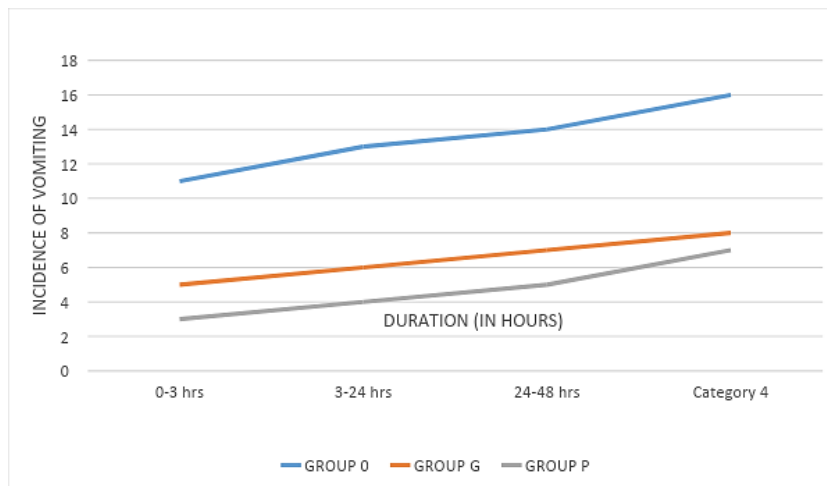
Table 4: Incidence of vomiting in three study groups

	Group O n (%)	Group G n (%)	Group P n (%)	P value
0-3 hrs	11(22)	5(10)	3(6)	0.043
3-24 hrs	13(26)	6(12)	4(8)	0.032
24-48 hrs	14(28)	7(14)	5(10)	0.044
48-72 hrs	16(32)	8(16)	7(14)	0.03

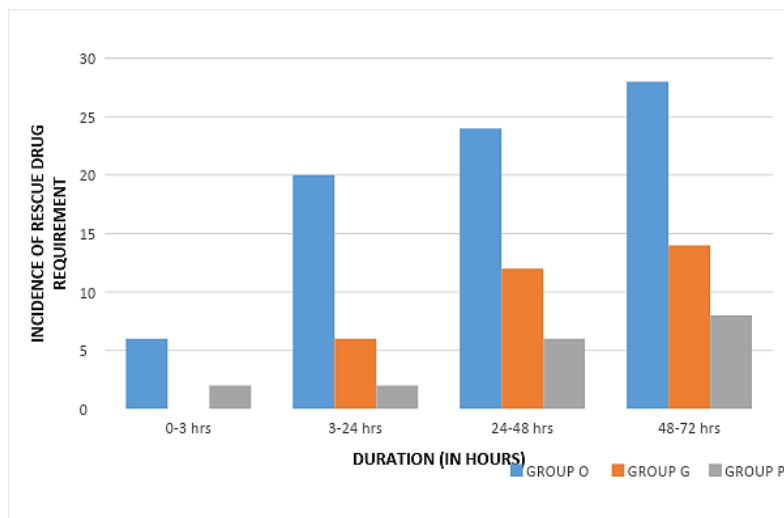
Graph 1



Graph 2



Graph 3



Discussion

PONV is most common and distressing complication post surgery, with considerable medical and economic impact, and is associated with high levels patient discomfort and dissatisfaction.⁹

Postoperative nausea and vomiting is a serious issue in patients posted for laparoscopic cholecystectomy, with incidence as high as 46 to 72%.⁸

The overall incidence of PONV estimated to be 25% to 30% and severe PONV in 18% of all patients undergoing surgery.¹⁰

Incidence of nausea here means number of patients suffered from nausea, and not the frequency of nausea.

The incidence of emetic sequelae is most in the first 24 hours postoperative period in patients posted for gynaecological surgery under general anaesthesia; although aetiology of PONV is multifactorial in terms of age, female gender, grade of obesity, h/o of motion sickness, previous postoperative emesis episodes, anxiety, gastroparesis, pain, type of anaesthetic used, severity of hypotension and type and prolonged duration of surgery.^{11,12}

The serotonin 5HT₃ receptor antagonists are major advances in prophylaxis of PONV as they lack the major adverse effects of traditionally used antiemetic drugs.^{13,14}

Paventi et al in their dose ranging study of ondansetron concluded that single dose of 8 mg is superior than 4 mg in the prevention of PONV. In our stud, we therefore used inj. Ondansetron 8mg iv before induction of anaesthesia in group O.¹⁵

Fujii et al proved that the efficacy of granisetron 40µg/kg is similar to 60µg/kg granisetron for preventing PONV after major gynaecological surgeries. The dose of granisetron 2.5 mg (approx. 45µg/kg) we chose was within its effective dose range.¹⁶

In study by Kovac Al et al palanosetron in dose of 0.025 mg, 0.05 mg and 0.075 mg were compared, the dose of 0.075 mg dose was more effective to placebo for all end points during 24 hours. In addition, was associated with reduced episodes of emesis during first 72 hours, with most deduction

in the first 24 hours. Therefore, we decided to use the dose of 0.075 mg for our study group.¹⁷

While comparing data of our study we found that incidence of nausea was significant during all study intervals with $P < 0.05$ and during the 3 to 24 hours, it was highest being 40% in group O and lowest being 14% in group P and was highly significant as p value was 0.0068.

While comparing the incidence of vomiting there was significant, difference with increased incidence in Ondansetron compared to Granisetron and Palanosetron throughout the observation period; least incidence of vomiting found in Palanosetron group.

Gupta et al compared the efficacy of ondansetron, granisetron and palanosetron in patients undergoing laparoscopic cholecystectomy. The difference among three groups was significant for all observations showing that the incidence of PONV was maximal during the first four hours and was more in ondansetron group.¹⁸

Sharma et al in their comparative study between ondansetron, granisetron and palanosetron in 90 patients posted for laparoscopic cholecystectomy found that the incidence of nausea was only 10% in palanosetron group as opposed to 33% in granisetron group and 60% in ondansetron group. The incidence of vomiting was least in palanosetron group owing to 6.7% compared to 26.7% in granisetron group and 53.3% in ondansetron group. Overall vomiting was highest in ondansetron and least in palanosetron. The difference was statistically significant.¹⁹

We observed that complete response was maximum in palanosetron group in comparison to ndansetron group with statistically significant difference. Taninder et al studied comparison between ondansetron (8 mg) and palanosetron (0.075 mg) undergoing middle ear surgery found that palanosetron was better than ondansetron in prevention of PONV.²⁰

Further in our study Inj. ondansetron 8mg IV was given as rescue antiemetic for vomiting or persistent nausea if two or more episodes occurred within 24 hours. The need of

rescue antiemetic was least in palonosetron group with statistically significance.

Incidence of headache, dizziness and drowsiness results were in accordance with study conducted by Gupta et al in which incidence of adverse effects were more in ondansetron group, but no statistical significant difference among the groups. No patient required treatment for these side effects and gradually resolved on their own mostly after 24-48 hours. None of the patients had allergic episodes or other adverse effects related to study drugs.

Conclusion

In this study, we concluded that Palonosetron hydrochloride is more safe, potent and effective in preventing PONV with least requirement of rescue antiemetic's, in comparison to the other study drugs in gynaecological surgery under general anaesthesia.

Conflict of Interest: None.

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