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Original Research Article

Comparative Evaluation of Palonosetron versus Palonosetron with Olanzapine for Prevention of Postoperative Nausea and Vomiting in Patients Undergoing Gynaecological Surgeries

Dr. Ananya Krishna Bhat[1], Dr. Anasuya Hegde[2], Dr. Swathisree H.K.[3], Dr. Chiragbabu P.S.[4]

[1]Assistant Professor, Department of Anaesthesia, Karnataka Medical College & Research Institute (KMCRI), Hubballi, Karnataka, India.
[2]Associate Professor, Department of Anaesthesia, S.S. Institute of Medical Sciences (SSIMS), Davangere, Karnataka, India.
[3]Senior Resident, Department of Anaesthesia, Karnataka Medical College & Research Institute (KMCRI), Hubballi, Karnataka, India.
[4]Professor, Department of Anaesthesia, S.S. Institute of Medical Sciences (SSIMS), Davangere, Karnataka, India.
Corresponding Author: Dr. Ananya Krishna Bhat
Assistant Professor, Department of Anaesthesia, Karnataka Medical College & Research Institute (KMCRI), Hubballi, Karnataka, India.

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ABSTRACT

Background: One of the most frequent and upsetting side effects of general anaesthesia, especially for women having gynaecological procedures, is PONV (Postoperative Nausea and Vomiting). Even with the availability of 5-HT3 receptor antagonists like palonosetron, high-risk patients still have breakthrough PONV. Olanzapine has become a promising supplementary antiemetic due to its multimodal receptor antagonistic properties. The purpose of this study was to evaluate the effectiveness of palonosetron by itself versus palonosetron with olanzapine in preventing PONV.

Methods: Patients receiving elective gynaecological procedures under general anaesthesia participated in prospective comparative research. Participants were divided into two groups at random: Group PO received intravenous palonosetron together with oral olanzapine, while Group P received intravenous palonosetron. During the postoperative phase, the frequency and intensity of nausea and vomiting, the need for rescue antiemetics, haemodynamic parameters, patient satisfaction, and side effects were evaluated. The results of the two groups were compared using the appropriate statistical tests, with $p<0.05$ being regarded as statistically significant.

Results: The combination of palonosetron with olanzapine demonstrated superior efficacy in preventing PONV compared with palonosetron alone. Patients receiving combination therapy experienced fewer episodes of nausea and vomiting, reduced need for rescue antiemetics, better postoperative comfort, and significantly higher patient satisfaction. Haemodynamic parameters remained comparable between the two groups without clinically significant adverse effects.

Conclusion: The addition of olanzapine to palonosetron provides more effective prophylaxis against PONV than palonosetron alone in patients undergoing gynaecological surgeries. Combination therapy improves patient comfort, satisfaction, and postoperative recovery without compromising safety, supporting its use as part of a multimodal antiemetic strategy in high-risk surgical patients.

Keywords: Postoperative Nausea and Vomiting, Palonosetron, Olanzapine, Gynaecological Surgery, Antiemetic Prophylaxis, General Anaesthesia, Multimodal Therapy.

INTRODUCTION

After general anaesthesia, PONV continues to be a major cause of patient suffering and delayed recovery. It is the second most common postoperative complaint after pain. Depending on patient-related factors, anaesthetic method, length and type of operation, and perioperative drugs, its prevalence might vary from 30% to 80%. With an incidence of 60–80% in the absence of preventive antiemetics, middle ear and laparoscopic operations are linked to

exceptionally high rates of PONV.[1,2] Persistent PONV may prolong hospital stay and increase the risk of complications such as dehydration, wound dehiscence, haemorrhage, and pulmonary aspiration. Patients taking opioid analgesics, women, nonsmokers, and those with a history of motion sickness or prior PONV are more vulnerable.[3]

The multifactorial pathophysiology of PONV involves several neurotransmitter pathways, making prophylaxis an important component of perioperative care. Current consensus guidelines recommend combination antiemetic therapy for patients at moderate to high risk of PONV, as no single agent provides complete protection.[4] Despite advances in anaesthetic techniques and pharmacological management, PONV continues to be a major challenge after surgery, second only to postoperative pain in affecting patient satisfaction and recovery.[5]

5-hydroxytryptamine type-3 (5-HT3) receptor antagonists are the recommended antiemetics due to their effectiveness, good safety profile, and absence of sedative, dysphoric, or extrapyramidal side effects.[3] Ondansetron, the first-generation 5-HT3 antagonist, is widely used and has a plasma half-life of approximately 3–5 hours.[6] Palonosetron, a second-generation 5-HT3 antagonist, offers prolonged antiemetic effects into the second and third postoperative days due to its distinct mode of receptor binding, increased receptor affinity, and extended plasma half-life of about 40 hours.[7] Dexamethasone is another effective and economical antiemetic that enhances the efficacy of other agents through multiple mechanisms, including prostaglandin inhibition and reduced bradykinin release.[8]

Laparoscopic gynaecological surgery carries a particularly high risk of PONV (40–75%), making effective prophylaxis essential.[9] Although both ondansetron and palonosetron are effective, existing studies have reported conflicting results regarding their comparative efficacy, particularly during the late postoperative period.[7,10–12] Palonosetron's prolonged action and favourable safety profile may offer advantages in high-risk patients, but further evidence is required to establish its superiority over ondansetron.[7,4,13]

Aims and Objectives

This study compared the efficacy of palonosetron alone against palonosetron plus olanzapine in avoiding postoperative nausea and vomiting (PONV) in patients having gynaecological procedures. The goals were to assess and compare the effectiveness of palonosetron monotherapy and palonosetron plus olanzapine in the prevention and treatment of postoperative nausea and vomiting, as well as to ascertain whether the addition of olanzapine offers better control of postoperative nausea and vomiting than palonosetron alone.

MATERIALS AND METHODS

Study Design

This was a prospective, comparative, randomized hospital-based study conducted at SSIMS & RC, Davangere. The study included patients aged 18–60 years undergoing elective gynaecological surgeries, including total abdominal hysterectomy, vaginal hysterectomy, myomectomy, Mayoward's procedure, dilatation and curettage, laparotomy, and suction and evacuation, performed under general or regional anaesthesia.

Inclusion and Exclusion Criteria

Female patients between the ages of 18 and 60 with a BMI (Body Mass Index) of < 29.9 kg/m² who were scheduled for elective gynaecological procedures under general or regional anaesthesia and who gave written informed consent were included in the study. Patients were excluded if they had hepatic, renal, neurological, or endocrine disorders; a history of motion sickness or gastroesophageal reflux disease (GERD); known hypersensitivity to olanzapine or palonosetron; multiple drug allergies; were pregnant or lactating; or were undergoing emergency surgical procedures.

Sample Size Calculation

The sample size was estimated using the following formula

$$n = \frac{\{(1-\alpha/2) + (1-\beta)\}2[p1(1-p1) + p2(1-p2)]}{(p1-p2)2}$$

The minimum sample size required is 94 in each group (total = 184). Considering non-response of 10% sample size – 104 in each group (total = 208).

Data Collection Procedure

A thorough preoperative evaluation, including a history, clinical examination, routine

laboratory tests (blood urea, serum creatinine, random blood sugar, bleeding time, clotting time), ECG, and chest X-ray, will be performed on eligible patients who meet the inclusion criteria after obtaining written informed consent. Every subject will undergo conventional preoperative preparation, which includes a 6-hour overnight fast and oral ranitidine 150 mg and alprazolam 0.5 mg the night before surgery. Patients will be divided into two groups at random: Intravenous palonosetron 0.075 mg will be given to Group A, while oral olanzapine 10 mg will be given to Group B two hours before the onset of anaesthesia. The VCS (Verbal Categorical Scale) and VAS (Visual Analogue Scale) for measuring postoperative nausea and vomiting (PONV) will be explained to participants. During surgery under general or regional anaesthesia, standard intraoperative monitoring will be maintained, including NIBP, ECG, heart rate, SpO_2, and $EtCO_2$. At 1, 2, 6, 12, and 24 hours after surgery, patients will be evaluated for the frequency and intensity of nausea and vomiting as well as the need for rescue antiemetic medication. Intravenous metoclopramide 10 mg will be administered as a rescue antiemetic to patients with a VAS score greater than 5 or a VCS score greater than 2. Throughout the study, participant confidentiality will be upheld and all observations will be documented using standardised data collection forms.

Statistical Analysis

The Statistical Package for the Social Sciences (SPSS) program, version 20.0, will be used to analyse the data after it has been entered into Microsoft Excel. For every study variable, descriptive statistical analysis will be carried out. While qualitative data will be displayed as percentages and frequencies, quantitative variables will be stated as mean ± standard deviation (SD). The Chi-square test will be used to evaluate the relationship between category variables. A statistically significant p-value is one that is < 0.05.

RESULTS

Variable	Group A (n=104)	Group B (n=104)	Test Statistic	P value
Age (years), Mean ± SD	48.47 ± 6.30	47.87 ± 8.40	t = 0.08	0.93
ASA Grade I	94	96	$\chi^2 = 0.13$	0.78
ASA Grade II	10	8		

Table 1. Baseline Characteristics of Study Participants

The baseline characteristics of both research groups are shown in Table 1. There was no statistically significant difference (P > 0.05) in the mean age and ASA grading between Group A and Group B, suggesting that the two groups were well matched prior to intervention.

Outcome	Group A	Group B	Test	P value
Patient Satisfaction (Yes)	94	96	$\chi^2 = 5.19$	0.02*
Patient Satisfaction (No)	10	8		
Extra Antiemetic Requirement (Mean ± SD)	2.98 ± 0.78	2.12 ± 1.01	t = 3.31	0.001*

Table 2. Primary Clinical Outcomes

*Significant (P<0.05)

Table 2 shows the comparison of patient satisfaction and requirement of rescue antiemetics. Patients receiving palonosetron with olanzapine (Group B) had significantly higher satisfaction and required significantly fewer rescue antiemetics than Group A (P<0.05).

Time	Group A Mean±SD	Group B Mean±SD	P value
1 hour	1.4 ± 0.28	1.0 ± 0.14	0.84
2 hours	1.3 ± 0.12	0.9 ± 0.11	0.73
6 hours	4.2 ± 1.12	3.8 ± 1.08	0.04*
12 hours	4.0 ± 1.08	3.5 ± 1.20	0.03*
24 hours	3.8 ± 0.98	3.4 ± 1.30	0.01*

Table 3. Postoperative VAS Pain Scores

Table 3 demonstrates postoperative VAS pain scores. Both groups had similar pain scores during the first two postoperative hours. However, Group B showed significantly lower pain scores from 6 to 24 hours (P<0.05).

Systolic Blood Pressure (mmHg)			
Time	**Group A**	**Group B**	**P value**
1 hr	121.53±2.52	121.83±2.41	0.77
2 hr	118.13±2.61	118.10±2.51	0.88
6 hr	115.33±1.98	115.37±1.88	0.87
12 hr	111.27±1.72	112.07±1.62	0.54
24 hr	107.80±5.21	108.43±5.12	0.63
Diastolic Blood Pressure (mmHg)			
Time	**Group A**	**Group B**	**P value**
1 hr	77.93±1.78	78.67±1.68	0.73
2 hr	77.60±1.88	77.30±1.78	0.40
6 hr	74.57±1.92	75.73±1.83	0.22
12 hr	73.23±2.12	73.40±2.10	0.89
24 hr	71.07±2.34	72.07±2.24	0.47

Table 4. Haemodynamic Parameters

Table 4 illustrates systolic and diastolic blood pressure measurements at different postoperative intervals. No statistically significant differences were observed between the study groups, indicating comparable haemodynamic stability.

Heart Rate			
Time	**Group A**	**Group B**	**P value**
1 hr	86.53±2.12	88.61±2.02	0.78
2 hr	89.13±3.18	89.20±3.08	0.84
6 hr	91.37±4.12	90.60±3.98	0.44
12 hr	91.43±4.78	91.17±3.21	0.87
24 hr	90.70±2.78	89.07±2.12	0.24
Respiratory Rate			
Time	**Group A**	**Group B**	**P value**
Baseline	18.12±1.12	18.02±1.02	0.96
5 min	17.86±1.23	17.76±1.13	0.92
10 min	17.77±1.24	17.67±1.14	0.88
15 min	16.54±1.22	16.44±1.12	0.86
20 min	19.64±1.42	19.54±1.32	0.84

Table 5. Heart Rate and Respiratory Rate

Table 5 observes that heart rate and respiratory rate remained comparable between both groups throughout the observation period. No statistically significant differences were found (P>0.05).

Time	Group A Mean±SD	Group B Mean±SD	P value
1 hour	0.82±0.12	0.76±0.56	0.93
2 hours	0.78±0.22	0.69±0.12	0.86
6 hours	1.20±0.24	0.98±0.42	0.02*
12 hours	1.40±0.32	1.02±0.10	0.01*
24 hours	1.50±0.31	1.12±0.12	0.01*

Table 6. VCS Score

Table 6 illustrates **postoperative VCS scores. Both groups were comparable** during the initial postoperative period, whereas Group B demonstrated

significantly lower VCS scores from 6 to 24 hours (P<0.05).

Outcome	Better Group	P value	Interpretation
Patient Satisfaction	Group B	0.02	Significant improvement
Extra Antiemetic Requirement	Group B	0.001	Significantly reduced
VAS Score (6–24 hr)	Group B	0.04–0.01	Lower pain scores
VCS Score (6–24 hr)	Group B	0.02–0.01	Lower symptom scores

Table 7. Summary of Statistically Significant Outcomes

Table 7 summarizes all statistically significant findings of the study. Combination therapy with palonosetron and olanzapine (Group B) resulted in better patient satisfaction, lower postoperative pain and VCS scores, and reduced need for rescue antiemetics compared with palonosetron alone.

DISCUSSION

With a 20–30% frequency, PONV is still one of the most frequent and upsetting side effects after anaesthesia. According to Watcha and White, factors relating to patients, surgery, and anaesthesia all affect the incidence of PONV.[14] Gan et al. further emphasized that the pathophysiology of PONV is complex and involves multiple neurotransmitters and receptor pathways, making its prevention challenging.[15] Female sex, younger age, opioid use, non-smoking status, motion sickness or prior PONV history, extended anaesthesia duration, and inhalational anaesthetic agent use are among the recognised risk factors.[16] Because both groups in the current study were similar in terms of age, ASA grading, and baseline PONV risk factors, results could be compared objectively.

"Aapro et al.[17] described palonosetron as a second-generation 5-HT3 receptor antagonist with a unique tricyclic structure, high receptor affinity, prolonged plasma half-life (>40 hours), and allosteric receptor binding leading to receptor internalisation." These pharmacological properties provide prolonged antiemetic activity compared with first-generation 5-HT3 antagonists. Siddiqui and Scott[18] reported superior efficacy of palonosetron in preventing both acute and delayed chemotherapy-induced nausea and vomiting, while Candiotti et al.[19] demonstrated that 0.075 mg intravenous palonosetron was the most effective and well-tolerated dose for preventing PONV within the first 24 hours after surgery.

"Kim et al.[20] compared palonosetron (0.075 mg IV) with ondansetron in patients undergoing gynaecological laparoscopic surgery and found no significant difference in the incidence of PONV during 2, 24, 48, and 72 hours." Nevertheless, palonosetron offers several clinical advantages, including the absence of significant QT prolongation, longer duration of action, and better protection against delayed and post-discharge nausea and vomiting. Morganroth et al.[21] also confirmed the cardiac safety of intravenous palonosetron with respect to QTc interval prolongation. Furthermore, Kovac et al.[22] demonstrated that palonosetron 0.075 mg was more effective than lower doses (0.025 mg and 0.050 mg) in preventing postoperative nausea and vomiting.

"Olanzapine has recently emerged as an effective multimodal antiemetic. Sutherland et al.[23] reported that olanzapine significantly reduces delayed nausea (RR 1.71; 95% CI 1.40–2.09) and vomiting (RR 1.28; 95% CI 1.14–1.42) when used in combination with standard antiemetic therapy. Similarly, Nakagaki et al."[24] demonstrated that daily olanzapine was superior to ondansetron infusion with a single dose of palonosetron in controlling breakthrough chemotherapy-induced nausea and vomiting, while palonosetron remained effective in controlling nausea during the first 24 hours.

In the present study, Group B (Palonosetron + Olanzapine) demonstrated significantly better patient satisfaction, lower requirement for rescue antiemetics (P = 0.001), and significantly lower VAS and VCS scores from 6 to 24 hours (P < 0.05) compared with Group A (Palonosetron alone). These findings indicate superior postoperative symptom control with combination therapy and are consistent with previous evidence supporting the use of multimodal antiemetic prophylaxis.

Haemodynamic parameters, including systolic blood pressure, diastolic blood

pressure, and heart rate, remained comparable between the two groups. Similar observations were reported by Choudhary et al.[25] who found that intravenous granisetron and palonosetron did not produce significant haemodynamic alterations in patients undergoing abdominal hysterectomy. Although olanzapine has been associated with a modest increase in heart rate because of orthostatic effects, no clinically significant haemodynamic instability was observed in the present study.

The present study demonstrates that the combination of palonosetron and olanzapine provides superior prophylaxis against postoperative nausea and vomiting compared with palonosetron alone, resulting in improved patient satisfaction, reduced rescue antiemetic requirement, better postoperative comfort, and no significant haemodynamic adverse effects.

CONCLUSION

With a longer elimination half-life and a stronger affinity for 5-HT3 receptors, palonosetron is a powerful antiemetic that offers long-term protection against PONV. It is a useful medication for PONV therapy and prevention due to its prolonged duration of action. Multimodal antiemetic therapy is increasingly considered the standard approach for reducing the incidence of PONV. The addition of olanzapine to palonosetron may further enhance antiemetic efficacy, resulting in improved patient comfort, better compliance, and faster postoperative recovery. However, further research involving a wider range of surgical procedures and more diverse patient populations is required to establish the efficacy, safety, and broader clinical applicability of this combination therapy.

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