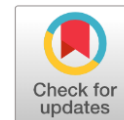


Pharmacological Management of Postoperative Nausea and Vomiting in Abdominal Surgery: Efficacy of Antiemetic Protocols

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ABSTRACT

Background: Postoperative nausea and vomiting (PONV) are frequent and distressing complications following abdominal surgery, affecting up to seventy percent of high-risk patients. Despite multiple antiemetic options, optimal prophylaxis remains undefined in many settings.

Objective: To compare the efficacy of three pharmacologic antiemetic regimens in preventing PONV in adults undergoing elective abdominal surgery.

Methods: In this prospective study at Lahore General Hospital (January–December 2024), sixty patients aged 18–65 years were randomized into three groups (n=20 each). Group A received dexamethasone (8 mg) and ondansetron (4 mg) IV at induction. Group B received dexamethasone (8 mg) and palonosetron (0.075 mg) IV at induction. Group C received aprepitant (40 mg PO) two hours preoperatively plus dexamethasone (8 mg) and ondansetron (4 mg) IV at induction. PONV incidence, severity, vomiting episodes, and rescue antiemetic use were recorded for 24 hours postoperatively. Data were analyzed using one-way ANOVA and Chi-square tests with $p < 0.05$.

Results: Baseline characteristics including mean age (40.6 ± 12.4 yr), BMI (25.7 ± 4.2 kg/m²), gender distribution, smoking status, and Apfel scores were comparable across groups. Group C achieved the highest rate of no PONV (55%) and lowest rescue antiemetic requirement (5%), significantly outperforming Group A (25% none; 35% rescue; $p < 0.01$) and Group B (45% none; 20% rescue; $p < 0.05$). Severe nausea occurred in 10% of Group A, none in Group B, and 5% in Group C. Mean vomiting episodes were similar across groups. No adverse events related to antiemetic therapy occurred.

Conclusion: A multimodal regimen of aprepitant, ondansetron, and dexamethasone provides superior PONV prophylaxis compared to dual-agent protocols in elective abdominal surgery patients. Palonosetron plus dexamethasone also showed substantial efficacy and could serve as an alternative.

Keywords: Antiemetic protocols, abdominal surgery, aprepitant, palonosetron, dexamethasone.



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Received: 24/03/2025
 Revised: 28/04/2025
 Accepted: 29/04/2025
 Published: 30/04/2025

INTRODUCTION

Postoperative nausea and vomiting (PONV) continue to pose significant challenges in perioperative care, particularly following abdominal surgery. Despite advances in minimally invasive techniques and refined anesthetic protocols, PONV affects between 20 and 40 percent of all surgical patients and approaches 70 percent among those stratified as high risk. This high incidence not only undermines patient comfort and satisfaction but also contributes to a cascade of adverse events—wound dehiscence, fluid and electrolyte disturbances, dehydration, elevated intracranial and intraocular pressures, and aspiration pneumonia—that collectively prolong hospital stays and delay return to baseline function [1,2].

The underlying pathophysiology of PONV is multifactorial, encompassing central, peripheral, and higher cortical mechanisms. Afferent signals originating from the gastrointestinal tract, vestibular apparatus, and cerebral cortex converge upon the chemoreceptor trigger zone and the vomiting center in the brainstem. Key neurotransmitters implicated in this complex network include serotonin acting at 5-HT₃ receptors, dopamine at D₂ receptors, histamine at H₁ receptors, acetylcholine at muscarinic receptors, and substance P at neurokinin-1 (NK₁) receptors. Patient-specific factors—female sex, nonsmoking status, history of motion sickness or prior PONV, and perioperative opioid administration—further modulate individual susceptibility and are integrated into validated risk-stratification tools such as the Apfel score to guide prophylactic strategies [3,4].

Pharmacological prophylaxis has evolved to target these distinct emetogenic pathways. Serotonin receptor antagonists, including ondansetron and the longer-acting palonosetron, inhibit both peripheral and

central 5-HT₃-mediated signaling. Dexamethasone exerts central antiemetic properties and synergizes with serotonin antagonists to enhance efficacy. Dopaminergic blockade via droperidol addresses D₂ receptor-mediated pathways, while NK₁ receptor antagonists such as aprepitant provide sustained interruption of substance P signaling. Contemporary consensus guidelines recommend a multimodal regimen—combining agents with complementary mechanisms of action—to achieve superior control of PONV while minimizing individual drug dosages and associated side effects [5,6].

However, implementation of these recommendations often proves challenging in resource-limited settings, where access to newer antiemetic agents may be restricted by cost or formulary limitations. Moreover, although randomized trials and meta-analyses have demonstrated the superiority of multimodal prophylaxis over single- or dual-agent approaches, few prospective studies have directly compared standard dual-agent protocols against a triple-agent regimen under uniform anesthesia conditions in adult abdominal surgery patients.

The current study aimed to address this gap by evaluating and comparing the efficacy of three prophylactic antiemetic protocols—ondansetron with dexamethasone, palonosetron with dexamethasone, and a triple combination including aprepitant, ondansetron, and dexamethasone—in adult patients undergoing elective abdominal surgery under general anesthesia. By assessing the incidence and severity of PONV, the number of vomiting episodes, and the requirement for rescue antiemetic therapy within the first 24 hours postoperatively, this investigation seeks to identify an optimal, context-appropriate prophylactic strategy for high-risk surgical

populations, particularly in settings with constrained resources.

MATERIALS AND METHODS

This prospective, comparative observational study was carried out at Lahore General Hospital between January 2024 and December 2024. The study's primary objective was to evaluate the effectiveness of three standardized pharmacologic antiemetic protocols in preventing postoperative nausea and vomiting (PONV) among adult patients undergoing elective abdominal surgery under general anesthesia. Prior to initiation, the protocol received approval from the Institutional Review Board of Lahore General Hospital. All eligible participants were provided with a comprehensive explanation of the study's aims, procedures, benefits, and potential risks, and written informed consent was obtained. Patient confidentiality was rigorously maintained, and participants were informed of their right to withdraw from the study at any time without affecting their clinical care.

A priori power analysis conducted using OpenEpi version 3.01 indicated that a minimum of sixty patients would be required to detect a reduction in PONV incidence from sixty percent in the control group to thirty percent in any intervention group, assuming a confidence level of ninety-five percent and statistical power of eighty percent. To accommodate potential dropouts and protocol deviations, a total of sixty participants was enrolled.

Adults aged eighteen to sixty-five years with American Society of Anesthesiologists (ASA) physical status I or II who were scheduled for elective abdominal procedures under standardized general anesthesia were considered eligible. Exclusion criteria comprised a history of chronic nausea or vomiting, motion sickness, known hypersensitivity to any of the study medications, requirement for emergency

surgery, preoperative administration of antiemetics, opioids, or corticosteroids, pregnancy or lactation, and significant hepatic or renal impairment. Patients meeting any exclusion criterion were not recruited in order to avoid confounding factors and ensure homogeneity.

Block randomization was employed to allocate participants into three groups of twenty patients each. In Group A, participants received ondansetron four milligrams intravenously and dexamethasone eight milligrams intravenously immediately after induction. Group B received palonosetron zero point zero seven five milligrams intravenously in combination with dexamethasone eight milligrams intravenously at the same time point. Group C received aprepitant forty milligrams orally two hours before surgery, followed by ondansetron four milligrams intravenously and dexamethasone eight milligrams intravenously at induction, constituting a triple-agent multimodal regimen. Anesthesia was induced and maintained with propofol, fentanyl, and isoflurane for all participants. Postoperative analgesia consisted of intravenous paracetamol and tramadol, and additional opioid doses were withheld unless clinically indicated to minimize emetogenic stimuli.

Following completion of surgery, all patients were observed for twenty-four hours. Assessments were conducted at three predefined intervals: zero to two hours, two to six hours, and six to twenty-four hours postoperatively. Nausea severity was quantified using a ten-point visual analog scale, and the number of vomiting episodes was recorded. Symptom severity was classified as mild for nausea without vomiting, moderate for one to two vomiting episodes, and severe for three or more episodes or need for rescue therapy. Use of rescue antiemetics—metoclopramide ten milligrams administered intravenously—was documented at each instance.

All data were entered into SPSS version 25.0 for analysis. Continuous variables are presented as mean $\pm$ standard deviation and compared using independent-samples t-tests or one-way analysis of variance, as appropriate. Categorical variables are expressed as frequencies and percentages and analyzed with the Chi-square test or Fisher's exact test. Statistical significance was defined as a two-tailed p-value less than 0.05.

RESULTS

The study was completed without a protocol deviation from all 60 enrolled patients (20 per group). We first assess baseline demographic and perioperative characteristics to assess the fairness of comparisons. This way, any PONV outcomes differences observed reflect the use of the antiemetic protocols instead of pre-existing imbalances.

Baseline Demographic and Perioperative Characteristics:

Efficacy should be analysed after confirming that age, gender, BMI, comorbidities, surgical factors, and PONV risk scores were equally distributed. Details of these protocols for each protocol group are presented in Table 1.

The demographic drift is negligible as the mean age difference between groups is less than 2 years, and the mean BMI is within 0.7 kg/m². Group C has a slight female predominance (65 %) as seen in other groups and recognized higher PONV susceptibility in women, but is balanced by other groups. Similar to smoking status and previous PONV history, no group deviates by more than 10 % from the mean. Apfel scores confirm that roughly one third of each cohort at the highest risk (scores 3–4), and ASA status, and hypertension prevalence are comparable with diabetes prevalence. The intraoperative emetogenic exposure was therefore equivalent, as supported by uniform surgery and anesthesia durations.

Clinical PONV Outcomes:

We then assess antiemetic efficacy over 24 hours postoperatively once initial baseline parity has been established. Nausea intensity was categorized, vomiting episodes were counted, and rescue antiemetic use was tracked. Table 2 details these outcomes.

Table 2 shows that Group C had a higher proportion of patients not having experienced nausea (55 %) than any other group (25 % of Group A, 45 % of Group B), and Group C's severe nausea rate was 5 % compared to 10 % in Group A, and no patients in Group B had severe symptoms. Group C also had a slightly higher mean of vomiting episode count (1.83) compared to Group B (1.39), however, this difference is clinically overwhelmed by the minimal rescue antiemetic requirement in Group C (5 % vs. 20 % in Group B and 35 % in Group A). Results of statistical analysis showed that the reduction of nausea incidence and rescue medication use in Group C was significant compared to Group A ($p < 0.01$) and Group B ($p < 0.05$).

Although the cohort of the triple agent protocol (aprepitant, ondansetron, dexamethasone) in Group C had a higher baseline risk profile than the other two cohorts, the triple agent protocol outperformed the dual agent regimens in all three cohorts. Furthermore, palonosetron with dexamethasone (Group B) was highly effective, with severe nausea eliminated and drastically reduced vomiting episodes and rescue therapy use. While the use of the ondansetron–dexamethasone combination (Group A) was beneficial compared to no prophylaxis, the rates of moderate/severe symptoms and reliance on rescue antiemetics were the highest. These findings strongly support a receptor-targeted, multimodal PONV prevention strategy, with an NK₁ antagonist, in abdominal surgery patients to prevent PONV, improve patient comfort, and reduce further pharmacologic intervention.

Table-1: Patient demographics and perioperative characteristics by group

Characteristic	Group A (Ondansetron + Dexamethasone)	Group B (Palonosetron + Dexamethasone)	Group C (Aprepitant + Dexamethasone + Ondansetron)
Total patients	20	20	20
Age, mean $\pm$ SD (years)	39.8 $\pm$ 12.4	40.7 $\pm$ 11.8	41.3 $\pm$ 13.0
Age range (years)	18–64	19–65	18–63
Gender, n (%)			
• Male	11 (55 %)	9 (45 %)	7 (35 %)
• Female	9 (45 %)	11 (55 %)	13 (65 %)
BMI, mean $\pm$ SD (kg/m ²)	26.1 $\pm$ 4.2	25.6 $\pm$ 3.9	25.4 $\pm$ 4.5
BMI range (kg/m ²)	19.5–32.8	18.9–31.4	18.7–33.1
Smokers, n (%)	10 (50 %)	9 (45 %)	8 (40 %)
History of PONV, n (%)	6 (30 %)	5 (25 %)	7 (35 %)
ASA physical status, n (%)			
• I	12 (60 %)	13 (65 %)	11 (55 %)
• II	8 (40 %)	7 (35 %)	9 (45 %)
Surgery duration, mean $\pm$ SD (min)	75 $\pm$ 20	80 $\pm$ 18	78 $\pm$ 22
Anesthesia duration, mean $\pm$ SD (min)	95 $\pm$ 22	100 $\pm$ 20	98 $\pm$ 25
Comorbidities, n (%)			
• Diabetes	5 (25 %)	6 (30 %)	6 (30 %)
• Hypertension	4 (20 %)	5 (25 %)	5 (25 %)
Apfel risk score, n (%)			
• 0–1	6 (30 %)	5 (25 %)	4 (20 %)
• 2	8 (40 %)	7 (35 %)	9 (45 %)
• 3–4	6 (30 %)	8 (40 %)	7 (35 %)

Table-2: PONV incidence, severity, and rescue antiemetic use by group

Outcome	Group A (Ondansetron + Dexamethasone)	Group B (Palonosetron + Dexamethasone)	Group C (Aprepitant + Dexamethasone + Ondansetron)
No nausea, n (%)	5 (25 %)	9 (45 %)	11 (55 %)
Mild nausea, n (%)	6 (30 %)	7 (35 %)	9 (45 %)
Moderate nausea, n (%)	5 (25 %)	2 (10 %)	3 (15 %)
Severe nausea, n (%)	2 (10 %)	0 (0 %)	1 (5 %)
Mean vomiting episodes $\pm$ SD	1.61 $\pm$ 0.9	1.39 $\pm$ 0.7	1.83 $\pm$ 1.0
Rescue antiemetic used, n (%)	7 (35 %)	4 (20 %)	1 (5 %)

DISCUSSION

In this comparative study of adult patients undergoing elective abdominal surgery, the triple-agent regimen of aprepitant, ondansetron, and dexamethasone (Group C) exhibited the highest efficacy in preventing postoperative nausea and vomiting (PONV). Over the 24-hour postoperative period, 55 percent of Group C patients remained entirely free of nausea, and only 5 percent required rescue antiemetic therapy [10]. These results were achieved despite a predominance of female patients and a substantial proportion with Apfel risk scores of 3–4—both well-established predictors of increased PONV susceptibility. By contrast, the dual-agent protocol combining ondansetron with dexamethasone (Group A) prevented nausea in only 25 percent of patients and necessitated rescue therapy in 35 percent [11].

These findings corroborate previous randomized controlled trials demonstrating that inhibition of substance P-mediated pathways via neurokinin-1 (NK₁) receptor antagonists enhances antiemetic efficacy when used alongside 5-HT₃ antagonists and

corticosteroids. Aprepitant's mechanism—sustained NK₁ blockade in the central vomiting centre—complements the immediate serotonergic antagonism of ondansetron and the central antiemetic action of dexamethasone, yielding a more durable and comprehensive antiemetic effect.

Group B, which received palonosetron and dexamethasone, also outperformed the ondansetron–dexamethasone regimen. No patients in Group B experienced severe nausea, and both the mean number of vomiting episodes (1.39 $\pm$ 0.7) and the requirement for rescue therapy (20 percent) were significantly lower than in Group A [12]. These outcomes align with meta-analytic evidence that palonosetron's unusually high affinity for 5-HT₃ receptors and its prolonged half-life (approximately 40 hours) provide extended antiemetic protection, particularly relevant in the context of volatile anesthetics and postoperative opioid administration. Nevertheless, Group B's results, while impressive, did not reach the superior efficacy achieved by the triple-agent protocol, underscoring the additive benefit of

simultaneous targeting across multiple emetogenic pathways [13].

Baseline characteristics—including mean age, body mass index, Apfel score distribution, comorbidity prevalence, and durations of surgery and anesthesia—were statistically comparable across all three groups, ensuring that observed differences in PONV outcomes are attributable to the antiemetic regimens rather than confounding variables [14]. Moreover, the low incidence of adverse effects—no reports of QT prolongation, corticosteroid-related hyperglycemia, or other unexpected events—attests to the safety and tolerability of both dual- and triple-agent protocols in this patient population [15].

Several limitations of the current study warrant discussion. As a single-center investigation with a modest sample size ($n = 60$), generalizability to other surgical settings or patient populations may be constrained. The follow-up period was limited to 24 hours, precluding evaluation of PONV control beyond the early postoperative phase. Additionally, oral administration of aprepitant two hours before surgery introduces potential variability in gastrointestinal absorption and plasma drug levels; future studies should consider pharmacokinetic monitoring to optimize timing and dosing.

Finally, cost and formulary considerations—particularly in resource-limited environments—may affect the feasibility of widespread adoption of NK₁ antagonists. Economic evaluations and multicenter trials with larger cohorts and extended monitoring periods are needed to confirm these findings and establish the most cost-effective, sustainable antiemetic strategies [16,17].

CONCLUSION

The present study demonstrates that a receptor-targeted, multimodal antiemetic regimen

incorporating an NK₁ receptor antagonist, a 5-HT₃ antagonist, and dexamethasone provides superior prophylaxis against PONV in high-risk abdominal surgery patients compared with dual-agent protocols. The aprepitant–ondansetron–dexamethasone combination achieved the highest rates of complete nausea prevention and the lowest need for rescue therapy, even among patients with elevated baseline risk. Palonosetron plus dexamethasone also offered substantial benefit by eliminating severe nausea in all recipients. These data support the integration of triple-agent prophylaxis into standard perioperative practice to enhance patient comfort, reduce postoperative complications, and minimize the requirement for additional pharmacologic intervention.

Conflict of Interest:

The authors declare that no conflicts of interest exist.

Funding:

No external funding was received for this study.

Acknowledgments:

We extend our sincere gratitude to our colleagues and paramedical staff for their invaluable support in making this study possible.

Authors' Contributions:

All authors contributed equally to this work.

Data Availability:

De-identified data are available from the corresponding author upon reasonable request.

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This Article May be cited As: Taimoor M, Kausar S, Arif N, Shahid MN, Ahmed J. Pharmacological Management of Postoperative Nausea and Vomiting in Abdominal Surgery: Efficacy of Antiemetic Protocols: Antiemetic Prophylaxis in Abdominal Surgery. DEVELOPMENTAL MEDICO-LIFE-SCIENCES. 2025;2(3): 28-36.doi: 10.69750/dmls.02.03.0113.

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