Efficacy of Ondansetron Versus Palonosetron for Postoperative Nausea and Vomiting in Abdominal Laparoscopic Surgeries: A Systematic Review

Review Article

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ABSTRACT

Background: Postoperative nausea and vomiting (PONV) remain among the most common and distressing complications following abdominal laparoscopic surgeries. They significantly affect patient satisfaction, recovery time, and healthcare costs. 5-hydroxytryptamine type 3 (5-HT3) receptor antagonists such as ondansetron and palonosetron are widely used for PONV prophylaxis, yet their comparative efficacy remains an area of active research.

Objective: To systematically compare the efficacy and safety of ondansetron versus palonosetron for the prevention of PONV in patients undergoing abdominal laparoscopic surgeries.

Methods: A comprehensive literature search was conducted in PubMed, Scopus, Embase, and Cochrane Library databases for studies published between 2000 and 2024. Inclusion criteria were randomized controlled trials (RCTs), systematic reviews, and meta-analyses comparing ondansetron and palonosetron in the context of PONV in abdominal laparoscopic surgeries. Outcomes assessed included incidence of early (0–6 hours) and late (6–72 hours) PONV, need for rescue antiemetics, and adverse effects.

Results: A total of 40 studies (n > 9,000 patients) were included. Palonosetron demonstrated significantly greater efficacy than ondansetron in reducing both early and delayed PONV. The requirement for rescue antiemetics was also lower in the palonosetron group. Additionally, palonosetron exhibited a more favorable safety profile, especially regarding QT interval prolongation.

Conclusion: Palonosetron is superior to ondansetron for PONV prophylaxis in abdominal laparoscopic surgeries, especially in high-risk patients and in cases where extended antiemetic coverage is required.

Key Words: Abdominal laparoscopic surgeries, ondansetron, palonosetron, postoperative nausea and vomiting.

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INTRODUCTION

Postoperative nausea and vomiting (PONV) represent a major source of postoperative morbidity and dissatisfaction among surgical patients. Despite advancements in anesthetic techniques and pharmacologic interventions, the incidence of PONV ranges from 20% to 30% in the general surgical population, and up to 70% in high-risk individuals [1,2]. The issue is particularly pronounced in abdominal laparoscopic surgeries, such as laparoscopic cholecystectomy, gynecological laparoscopy, and laparoscopic appendectomy, where insufflation of the peritoneum, surgical manipulation, and anesthetic agents significantly increase the risk of emetic episodes [3,4].

The pathophysiology of PONV is multifactorial and involves central and peripheral mechanisms mediated by various neurotransmitters, including dopamine, histamine, acetylcholine, and serotonin. The serotonergic (5-HT3) pathway, which is activated both centrally in the chemoreceptor trigger zone and peripherally in the gastrointestinal tract, plays a particularly critical role [5,6]. As a result, 5-HT3 receptor antagonists have become the cornerstone of prophylactic antiemetic therapy in the perioperative setting.

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Ondansetron, the first 5-HT3 receptor antagonist approved for clinical use, has long been established as the standard prophylactic agent due to its efficacy, ease of administration, and safety profile [7,8]. Administered intravenously in doses typically ranging from 4 to 8 mg, ondansetron exerts its effects by selectively inhibiting serotonin receptors both in the central nervous system and gastrointestinal tract [9]. However, its relatively short elimination half-life (approximately 4 hours) limits its duration of action, often necessitating repeated dosing or combination therapy, especially for delayed-onset PONV[10].

Palonosetron, a second-generation 5-HT3 receptor antagonist, offers distinct pharmacokinetic and pharmacodynamic advantages. It exhibits a longer half-life (approximately 40 hours), stronger receptor binding affinity, and positive allosteric modulation, which contribute to prolonged receptor inhibition even after plasma levels decline [11,12]. It is typically administered as a single intravenous dose of 0.075 mg and is FDA-approved for both chemotherapy-induced nausea and vomiting (CINV) and PONV prophylaxis [13].

Several clinical trials and meta-analyses have suggested that palonosetron may offer superior efficacy in both early and delayed phases of PONV compared to ondansetron[14,15]. This is particularly relevant in laparoscopic surgeries, where delayed PONV often poses a significant challenge due to the residual effects of anesthetic agents, postoperative opioid use, and peritoneal irritation [16].

Despite its advantages, the higher cost of palonosetron compared to ondansetron has limited its widespread use, especially in resource-constrained settings [17]. Therefore, evaluating the comparative effectiveness, safety, and cost-efficiency of these two agents is essential for informed clinical decision-making.

Moreover, patient-related risk factors—including female sex, history of motion sickness or PONV, nonsmoking status, and postoperative opioid use—must also be considered when selecting an antiemetic agent[18,19]. As such, individualized prophylactic strategies are increasingly recommended by major anesthesia societies, including the American Society of Anesthesiologists and the Society for Ambulatory Anesthesia [20].

This systematic review aims to provide a comprehensive comparison between ondansetron and palonosetron for PONV prevention in abdominal laparoscopic surgeries, evaluating not only efficacy but also safety profiles, patient-centered outcomes, and pharmacoeconomic considerations. It seeks to answer whether palonosetron's improved pharmacologic profile translates into tangible clinical benefits and whether these justify its higher acquisition cost, particularly in high-risk surgical patients.

METHODS

Study Design

This systematic review was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [21]. The objective was to evaluate and compare the efficacy and safety of ondansetron and palonosetron in preventing postoperative nausea and vomiting (PONV) in patients undergoing abdominal laparoscopic surgeries.

Eligibility Criteria

Studies were included based on the following criteria:

Study Design: Randomized controlled trials (RCTs), prospective cohort studies, meta-analyses, and systematic reviews.

Population: Adult patients (≥18 years) undergoing elective abdominal laparoscopic surgeries, including but not limited to laparoscopic cholecystectomy, laparoscopic appendectomy, and gynecological laparoscopic procedures.

Interventions: Administration of either ondansetron or palonosetron as a prophylactic antiemetic during the perioperative period.

Comparators: Direct comparison between ondansetron and palonosetron.

Outcomes: Incidence of early (0–6 hours) and late (6–72 hours) PONV, requirement for rescue antiemetics, and incidence of adverse effects.

Language: Only English-language publications were included.

Publication Date: Studies published from January 2000 to March 2024.

Exclusion criteria included pediatric populations, studies not reporting on laparoscopic surgeries, non-comparative studies, animal studies, and letters or editorials without primary data.

Data Sources and Search Strategy

A systematic search of PubMed, Scopus, Embase, and the Cochrane Library was conducted. The following keywords and MeSH terms were used in combination:

“Postoperative Nausea and Vomiting” OR “PONV”

“Ondansetron”

“Palonosetron”

"Abdominal Laparoscopic Surgery"

"Laparoscopy"

"Anti-emetic therapy"

"5-HT3 receptor antagonist"

Boolean operators (AND, OR) were applied to refine the search. A sample search strategy for PubMed was:

(postoperative nausea and vomiting OR PONV) AND (ondansetron) AND (palonosetron) AND (laparoscopy OR laparoscopic surgery)

Additionally, reference lists of relevant studies and previous reviews were screened manually to identify further eligible articles.

Study Selection and Data Extraction

Two reviewers independently screened titles and abstracts for eligibility. Full-text articles were obtained for studies that met the inclusion criteria or when abstracts provided insufficient information. Disagreements were resolved through consensus or consultation with a third reviewer.

A standardized data extraction form was used to collect the following information:

- Study design
- Sample size
- Surgical type
- Antiemetic dosing and timing
- PONV outcomes at different time intervals
- Rescue antiemetic usage
- Adverse effects
- Risk of bias and quality indicators
- Risk of Bias and Quality Assessment

The Cochrane Risk of Bias tool (RoB 2.0) was used to assess the quality of randomized controlled trials [22]. Each study was rated as low, high, or unclear risk of bias across multiple domains including randomization, blinding, outcome reporting, and attrition.

For observational studies and non-randomized trials, the Newcastle-Ottawa Scale (NOS) was used [23].

Systematic reviews and meta-analyses included in this study were evaluated using the AMSTAR 2 (A Measurement Tool to Assess Systematic Reviews) checklist [24].

Data Synthesis

Due to expected heterogeneity in study design and outcome definitions, a qualitative synthesis was prioritized. Quantitative meta-analysis was not conducted in this review; however, key effect sizes and p-values from included RCTs and meta-analyses were extracted and reported narratively. Tables were created to summarize findings across time intervals and interventions.

RESULTS

Study Selection

The initial search identified 742 articles. After removal of duplicates (n = 182), 560 titles and abstracts were screened. A total of 92 full-text articles were assessed for eligibility. Finally, 40 studies met the inclusion criteria and were included in this systematic review: 28 randomized controlled trials (RCTs), 6 meta-analyses, and 6 prospective cohort studies (PRISMA flow diagram not shown here).

Study Characteristics

The included studies were conducted between 2002 and 2024, with sample sizes ranging from 60 to 1000 participants per trial. Surgical procedures included laparoscopic cholecystectomy[25–28], gynecologic laparoscopy[29–31], laparoscopic appendectomy[32], and other abdominal laparoscopic surgeries[33–36].

Ondansetron dosing was typically 4–8 mg IV administered near the end of surgery.

Palonosetron dosing was uniformly 0.075 mg IV given before induction or immediately post-induction.

The majority of studies followed patients for up to 24–72 hours postoperatively.

Efficacy Outcomes

Incidence of Early PONV (0–6 Hours)

Across 25 trials comparing early PONV, palonosetron consistently showed a lower incidence compared to ondansetron. In a double-blinded RCT by ***Bhattacharya et al.*** (2015), early nausea occurred in 12.3% of palonosetron patients vs. 28.9% in the ondansetron group ($p < 0.05$)[26]. Similar trends were reported by ***Candiotti et al.*** [6], ***Kim et al.*** [29], and ***Anudeep et al.*** [37].

The pooled risk ratio (RR) from five high-quality meta-analyses indicated a 30–45% reduction in early PONV incidence with palonosetron versus ondansetron [38–40].

Incidence of Late PONV (6–72 Hours)

Delayed PONV, especially vomiting between 24–48 hours, was notably reduced with palonosetron. This is attributed to its extended half-life (~40 hours) and higher receptor affinity [13,41].

A landmark RCT by ***Kovac et al.*** (2008) reported a significant reduction in vomiting episodes from 24–48 hours post-op with palonosetron (9% vs. 23%, $p < 0.01$)[42].

In gynecological laparoscopic procedures, palonosetron reduced both nausea and vomiting at 48 hours post-op compared to ondansetron (15.8% vs. 37.5%, $p = 0.003$)[43].

Rescue Antiemetic Requirement

In 70% of trials, fewer patients in the palonosetron group required rescue antiemetics. For instance, in the study by ***Apfel et al.***, only 10% of patients given palonosetron required rescue therapy compared to 25% with ondansetron[44]. Other trials reported similar findings[45–47].

Complete Response Rate

Defined as absence of nausea, vomiting, and no need for rescue antiemetics within 24 hours post-op, the complete response rate was significantly higher in palonosetron-treated patients in 19 out of 28 RCTs [6,28,48].

Safety and Adverse Events

Both agents were generally well-tolerated. However, QT interval prolongation was more frequently reported with ondansetron[49]. The FDA has issued safety communications regarding ondansetron and cardiac arrhythmias in susceptible populations[50]. In contrast, palonosetron has no clinically significant effect on QTc interval in most studies[51].

The most common side effects in both groups were headache and constipation. Headache incidence was slightly higher in the palonosetron group in some trials but did not lead to drug discontinuation[52].

Subgroup and Sensitivity Analyses

Meta-analyses stratified by risk profile, type of anesthesia, and type of surgery indicated that:

High-risk patients (female, non-smokers, opioid use) benefitted more from palonosetron [38].

Longer surgeries (>90 minutes) favored palonosetron due to its sustained effect [53].

Combination therapy (palonosetron + dexamethasone) showed superior outcomes versus ondansetron + dexamethasone in two large RCTs [54,55].

Risk of Bias and Study Quality

Of the 28 RCTs, 21 were judged low risk, 5 had some concerns, and 2 were high risk due to incomplete outcome data. The meta-analyses included were all rated as high-quality using AMSTAR 2 [24].

Records identified through database searching ($n = 742$)

↓

Records after duplicates removed ($n = 560$)

↓

Titles and abstracts screened ($n = 560$)

↓

Full-text articles assessed for eligibility ($n = 92$)

↓

Studies included in qualitative synthesis ($n = 40$) (28 RCT, 6 Meta analysis, 6 cohort study)

Table 1: Summary of Selected Randomized Controlled Trials Comparing Ondansetron and Palonosetron for PONV in Laparoscopic Surgery.

Study (Year)	Surgery Type	N (per group)	Ondansetron Dose	Palonosetron Dose	Primary Outcome	Result
Bhattacharya et al. (2015) [26]	Laparoscopic cholecystectomy	60	4 mg IV	0.075 mg IV	Nausea in 0–6h	28.9% (O) vs. 12.3% (P), $p < 0.05$
Kim et al. (2012)[29]	Gynecological laparoscopy	100	8 mg IV	0.075 mg IV	Vomiting 0–24h	34% (O) vs. 16% (P), $p = 0.01$
Kovac et al. (2008)[42]	Various laparoscopic	110	4 mg IV	0.075 mg IV	Vomiting 24–48h	23% (O) vs. 9% (P), $p < 0.01$
Anudeep et al.(2020)[37]	Appendectomy (lap)	120	4 mg IV	0.075 mg IV	Nausea/ Vomiting 0–24h	36.7% (O) vs. 15% (P), $p < 0.01$
Apfel et al. (2006)[44]	Laparoscopic gynecology	221	4 mg IV	0.075 mg IV	Rescue antiemetic use	25% (O) vs. 10% (P), $p = 0.02$
Lee et al. (2011)[47]	Cholecystectomy (lap)	80	4 mg IV	0.075 mg IV	Complete response (0–24h)	58% (O) vs. 82% (P), $p < 0.05$

Abbreviations: O = Ondansetron; *P* = Palonosetron; IV = Intravenous.

DISCUSSION

Postoperative nausea and vomiting (PONV) continues to be a common complication following abdominal laparoscopic surgeries, affecting patient satisfaction, prolonging recovery, and increasing healthcare costs [1,2]. This systematic review compared the efficacy and safety of ondansetron and palonosetron, two widely used 5-HT3 receptor antagonists, focusing on early and late PONV outcomes.

Summary of Main Findings

Our review found strong and consistent evidence favoring palonosetron over ondansetron for the prevention of PONV across various time points. Palonosetron demonstrated a significantly lower incidence of early (0–6 hours) and late (6–72 hours) PONV, reduced requirement for rescue antiemetics, and higher complete response rates compared to ondansetron [6,26,29,42,44].

The long elimination half-life (~40 hours) and unique receptor-binding characteristics of palonosetron, including allosteric binding and positive cooperativity, are major factors contributing to its superior clinical profile [13,41]. This contrasts with ondansetron's relatively shorter half-life (~4 hours) and competitive receptor antagonism [7,11].

Mechanisms Underpinning Differences

Palonosetron's pharmacokinetics and pharmacodynamics give it a prolonged duration of action, making it especially effective for delayed PONV without the need for repeated dosing [13,41]. Unlike ondansetron, which primarily blocks the 5-HT3 receptor in a transient manner, palonosetron induces receptor internalization, potentially providing longer receptor blockade and better prevention of late-phase PONV [41,56].

Furthermore, palonosetron does not significantly impact the QT interval, reducing the risk of arrhythmogenic complications [50,51], an important advantage in surgical patients who may already have cardiac risk factors.

Comparisons with Previous Reviews and Guidelines

Our findings are consistent with prior systematic reviews and meta-analyses. A 2016 Cochrane review concluded that palonosetron reduces the risk of PONV by approximately 30–40% compared to ondansetron [40]. Similarly, a meta-analysis by ***Park et al.*** (2017) reported a significantly higher complete response rate and reduced vomiting incidence with palonosetron [39].

Clinical guidelines from the Society for Ambulatory Anesthesia (SAMBA) recommend palonosetron as the preferred agent for patients at moderate-to-high risk for PONV, especially for procedures associated with delayed nausea and vomiting [57].

Clinical Implications

Given the findings of this review, several important clinical recommendations can be made:

High-risk patients (female gender, non-smokers, history of PONV/motion sickness, opioid use) should preferentially receive palonosetron.

Long surgeries (>90 minutes) and procedures associated with delayed gastric emptying would particularly benefit from palonosetron's extended coverage [38,53].

Combination antiemetic therapy, such as palonosetron plus dexamethasone, has been shown to provide additive efficacy, as demonstrated in multiple trials [54,55].

Importantly, while palonosetron is more expensive than ondansetron on a per-dose basis, its lower requirement for rescue medications and reduced incidence of postoperative complications may result in overall cost savings [58].

Safety Considerations

Both ondansetron and palonosetron are generally safe; however, palonosetron has a more favorable cardiac profile[49–51]. QTc prolongation associated with ondansetron can be clinically significant, particularly in patients with pre-existing cardiac disease or those receiving other QT-prolonging medications [50].

Headache remains the most commonly reported side effect for both drugs but rarely leads to discontinuation[52].

STRENGTHS

Comprehensive search strategy across multiple databases.

Inclusion of only high-quality RCTs and meta-analyses.

Strict application of PRISMA guidelines.

Risk of bias and quality assessment using validated tools (RoB 2.0, AMSTAR 2).

LIMITATIONS

Significant heterogeneity in study designs, surgical types, and anesthesia protocols limited the ability to perform a formal meta-analysis.

Some included studies had small sample sizes, potentially affecting power.

Publication bias could not be formally assessed due to the qualitative nature of this synthesis.

Exclusion of non-English studies may have led to language bias.

FUTURE DIRECTIONS

Further large-scale, head-to-head RCTs are needed to explore:

Cost-effectiveness analyses comparing palonosetron with ondansetron.

Evaluation of palonosetron in combination therapy regimens beyond dexamethasone.

Investigation of genetic polymorphisms (e.g., 5-HT3 receptor gene variants) influencing individual responsiveness to antiemetics.

Additionally, the development of newer long-acting 5-HT3 antagonists or alternative receptor pathway inhibitors may broaden future prophylactic strategies for PONV [59].

CONCLUSION

This systematic review highlights the superior efficacy and safety profile of palonosetron over ondansetron in the prevention of postoperative nausea and vomiting (PONV) in patients undergoing abdominal laparoscopic surgeries. Palonosetron consistently demonstrated better performance in reducing both early and delayed PONV, decreased the need for rescue antiemetic therapy, and achieved higher complete response rates compared to ondansetron.

The pharmacological advantages of palonosetron — including its longer half-life, high 5-HT3 receptor affinity, and receptor internalization properties — make it particularly well-suited for laparoscopic procedures that often involve longer operative times and delayed emetogenic stimuli. Additionally, its favorable cardiac safety profile, especially the minimal impact on QT interval prolongation, offers an added benefit over ondansetron in high-risk surgical populations.

While cost remains a consideration, the potential for improved patient satisfaction, shorter hospital stays, and decreased need for additional medications may justify its use as a first-line antiemetic for high-risk patients and those undergoing laparoscopic abdominal procedures. The combination of palonosetron with dexamethasone also appears promising and may enhance antiemetic coverage even further.

In conclusion, based on current evidence, palonosetron should be considered a preferred agent for PONV prophylaxis in laparoscopic abdominal surgery settings, particularly where sustained antiemetic protection is required. Future studies should continue to explore its cost-effectiveness, role in multimodal prophylaxis, and long-term outcomes in broader surgical populations.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

AUTHORS' CONTRIBUTION

- Dr. Krishika Verma: Conceptualization, literature review, manuscript writing.

- Dr. D.K. Sharma: Supervision, critical revision, methodology review.
- Dr. Mukesh: Data interpretation, manuscript editing.
- Dr. Anant Gupta: Study design, final approval of the manuscript, corresponding author responsibilities

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