



# Effect of antiemetic co-administration with anesthesia on reducing postoperative nausea and vomiting

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## Abstract

Postoperative nausea and vomiting (PONV) remain among the most common and distressing complications following anesthesia and surgery, affecting up to 30% of patients and substantially impacting recovery and patient satisfaction. The co-administration of antiemetic agents with anesthetic drugs has emerged as a critical strategy to mitigate this issue. This article reviews current evidence on the effectiveness of antiemetic co-administration with anesthesia in reducing PONV, drawing upon clinical trials, meta-analyses, and case studies. It evaluates key pharmacologic agents such as 5-HT<sub>3</sub> receptor antagonists, corticosteroids, dopamine antagonists, and the role of anesthetic choice, particularly propofol-based regimens. The findings indicate that multimodal antiemetic protocols integrated with anesthesia significantly reduce the incidence and severity of PONV. Clinical practice implications, challenges, and future research directions are discussed to guide optimized perioperative care.

**Keywords:** postoperative nausea and vomiting, antiemetics, anesthesia, propofol, ondansetron, dexamethasone, multimodal therapy, rescue antiemetics, patient outcomes, clinical studies, PONV prevention

## 1. Introduction

Postoperative nausea and vomiting (PONV) is a pervasive complication following surgical procedures performed under general or regional anesthesia. Despite advances in anesthetic techniques and perioperative care, the incidence of PONV remains stubbornly high, affecting approximately 20% to 30% of the general surgical population and up to 80% of patients identified as high risk. This distressing condition not only causes significant patient discomfort and dissatisfaction but also contributes to delayed recovery, prolonged hospital stays, increased healthcare costs, and in some cases, serious complications such as dehydration, electrolyte imbalance, wound dehiscence, and aspiration pneumonia.

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The pathophysiology of PONV is multifactorial, involving complex interactions between patient-specific factors, anesthetic agents, surgical stimuli, and postoperative management. Known patient risk factors include female sex, nonsmoking status, history of motion sickness or previous PONV, and the use of postoperative opioids. Anesthetic agents, particularly volatile inhalational anesthetics and opioids, are major contributors to PONV as they stimulate chemoreceptor trigger zones and vagal afferents, triggering nausea and vomiting pathways in the central nervous system.

Over the past few decades, significant efforts have been made to reduce the burden of PONV through pharmacologic prophylaxis and improved anesthesia practices. Antiemetic drugs, such as 5-hydroxytryptamine type 3 (5-HT<sub>3</sub>) receptor antagonists (e.g., ondansetron), corticosteroids (e.g., dexamethasone), dopamine antagonists (e.g., droperidol), and neurokinin-1 receptor antagonists, have become mainstays in the prevention and treatment of PONV. However, their efficacy is often optimized when used in conjunction with anesthetic techniques that inherently reduce PONV risk.

Intravenous anesthetics, particularly propofol, have been shown to possess intrinsic antiemetic properties, providing an additional layer of protection against PONV when used as

part of balanced anesthesia or total intravenous anesthesia (TIVA). The co-administration of antiemetic agents with anesthesia—termed multimodal prophylaxis—has emerged as a best practice strategy to synergistically reduce the incidence and severity of PONV.

This article aims to provide a comprehensive review of current evidence regarding the effect of antiemetic co-administration with anesthesia on reducing postoperative nausea and vomiting. Through analysis of randomized controlled trials, meta-analyses, and clinical case studies, it explores the pharmacologic mechanisms, anesthetic choices, timing of administration, and clinical outcomes associated with these interventions. Additionally, the article discusses practical considerations for integrating multimodal antiemetic protocols into perioperative care pathways, highlighting challenges and opportunities for optimizing patient-centered outcomes.

Improving the management of PONV not only alleviates patient suffering but also enhances recovery trajectories, reduces unplanned hospital admissions, and promotes more efficient use of healthcare resources. As surgical volumes and patient complexity continue to rise, the role of antiemetic co-administration in anesthesia will remain a focal point in advancing perioperative medicine and improving the quality of surgical care.

## 2. Methodology

This study undertook a systematic and comprehensive review of the existing literature to evaluate the effect of antiemetic co-administration with anesthesia on the incidence and severity of postoperative nausea and vomiting (PONV). The methodology was designed to ensure a rigorous, unbiased synthesis of current clinical evidence spanning multiple research designs and patient populations.

A structured search strategy was implemented across three major biomedical and healthcare databases: PubMed, Cochrane Library, and Embase. The search period was limited from January 2008 to April 2024 to capture contemporary anesthetic techniques, pharmacologic advancements, and evolving clinical practices.

The search terms included a combination of Medical Subject Headings (MeSH) and free-text keywords such as “postoperative nausea and vomiting,” “PONV,” “antiemetic co-administration,” “anesthesia,” “propofol,” “ondansetron,” “dexamethasone,” “multimodal antiemetic therapy,” “perioperative care,” and “rescue antiemetics.”

Inclusion criteria were predefined to enhance the relevance and quality of the evidence base. Studies eligible for inclusion were original randomized controlled trials (RCTs), systematic reviews, meta-analyses, prospective and retrospective observational cohort studies, and clinical case series that investigated the prophylactic or therapeutic use of antiemetics administered concurrently with anesthetic agents in surgical patients. The primary outcomes of interest included incidence and severity of PONV, need for rescue antiemetic therapy, patient satisfaction, and adverse events related to antiemetic use. Studies focusing exclusively on pediatric populations, non-surgical nausea, or non-human subjects were excluded to maintain clinical applicability.

After removal of duplicates, two independent reviewers conducted title and abstract screening to identify potentially relevant articles. Full-text review was then performed to confirm eligibility based on inclusion and exclusion criteria. Discrepancies in study selection were resolved through consensus or consultation with a third reviewer to minimize selection bias.

Data extraction was performed using a standardized form capturing key study characteristics such as authorship, year of publication, sample size, surgical procedure type, anesthesia and antiemetic regimens, timing and dosage of agents, outcome measures, and reported adverse effects. Particular emphasis was placed on studies that detailed the co-administration of antiemetics with different anesthetic modalities, including total intravenous anesthesia (TIVA) with propofol and volatile inhalational agents.

Quality assessment of included studies was conducted using established tools: the Cochrane Risk of Bias tool for randomized trials

the Newcastle-Ottawa Scale for observational studies. These assessments informed the weight given to individual studies during qualitative synthesis.

In addition to the literature review, clinical case studies and institutional quality improvement reports were analyzed to provide real-world insights into the implementation and effectiveness of multimodal antiemetic protocols in perioperative settings. This mixed-methods approach allowed the integration of quantitative evidence with qualitative experiences, enriching the contextual understanding of antiemetic co-administration's impact on PONV.

The collated data were synthesized narratively, highlighting trends in efficacy, safety, timing, and patient-centered outcomes. Where appropriate, quantitative data from meta-analyses were summarized to support evidence-based conclusions. The methodology ensured a comprehensive appraisal of the literature, enabling robust recommendations for clinical practice and future research.

### 3. Literature Review

Postoperative nausea and vomiting (PONV) remains a significant clinical challenge despite decades of research and evolving perioperative management strategies. The literature reveals a consensus that PONV is a multifactorial phenomenon, influenced by patient-specific risk factors, surgical procedures, anesthetic techniques, and pharmacologic interventions. This complexity has driven extensive investigation into the most effective methods for prophylaxis and treatment, with a growing focus on the synergistic effects of antiemetic co-administration alongside anesthesia.

Early studies established the association between volatile inhalational anesthetics and increased PONV incidence. Apfel et al. (2002) demonstrated that volatile agents, such as sevoflurane and isoflurane, significantly elevate the risk of PONV compared to total intravenous anesthesia (TIVA) with propofol. Propofol's intrinsic antiemetic properties have since been extensively documented. White et al. (2003) highlighted that propofol reduces the incidence of PONV by inhibiting central nervous system emetic pathways, particularly when used as a continuous infusion or within TIVA protocols. Its use has become a cornerstone of multimodal anesthetic regimens aiming to minimize PONV.

Pharmacologic agents targeting specific emetic pathways have revolutionized PONV management. Among these, 5-hydroxytryptamine type 3 (5-HT<sub>3</sub>) receptor antagonists, especially ondansetron, have been the most extensively studied and widely adopted. Ondansetron functions by blocking serotonin receptors centrally and peripherally, thereby mitigating nausea and vomiting signals. Kovac (2000) summarized multiple randomized controlled trials indicating a consistent 25% to 30% reduction in PONV incidence with ondansetron prophylaxis, establishing it as a first-line agent.

Corticosteroids, in particular dexamethasone, have demonstrated significant additive benefits when combined with 5-HT<sub>3</sub> antagonists. Their antiemetic mechanism appears to involve modulation of inflammatory mediators and suppression of prostaglandin synthesis, contributing to decreased emetic signaling. Meta-analyses by Gan et al. (2007) revealed that dexamethasone alone reduces PONV risk by approximately 20%, and when combined with ondansetron, the incidence of PONV decreases by nearly 50%. This synergistic effect has informed clinical guidelines recommending multimodal antiemetic prophylaxis in patients at moderate to high risk.

Dopamine receptor antagonists, such as droperidol, have historically been effective in PONV prevention; however, safety concerns related to QT prolongation and extrapyramidal symptoms have curtailed their routine use. More recently, neurokinin-1 (NK1) receptor antagonists like aprepitant have emerged as promising agents, particularly in high-risk populations, though their high cost and limited availability have restricted widespread adoption.

The timing of antiemetic administration has also been recognized as a critical factor influencing efficacy. Studies indicate that pre-induction or early intraoperative administration of agents like ondansetron and dexamethasone enhances receptor occupancy and prophylactic effectiveness compared to postoperative dosing. For example, a randomized controlled trial by Gan et al. (2007) demonstrated superior outcomes when ondansetron was administered 15 minutes before incision.

Clinical practice guidelines, including those from the Society for Ambulatory Anesthesia (SAMBA), advocate for risk stratification using tools like the Apfel score to tailor prophylaxis. Patients with multiple risk factors benefit most from combined anesthetic and pharmacologic approaches, integrating propofol-based anesthesia with dual or triple antiemetic therapy targeting multiple receptor systems.

Despite significant advances, the literature acknowledges persistent challenges. Variability in surgical types, patient populations, and outcome measures complicates direct comparisons across studies. Additionally, the risk of adverse effects, including headache, dizziness, and rare cardiac events, necessitates careful balancing of benefits and risks.

Emerging research explores novel strategies to further reduce PONV. These include the use of newer anesthetic agents with improved antiemetic profiles, personalized medicine approaches incorporating pharmacogenomics, and adjunctive non-pharmacologic interventions such as acupressure and hydration protocols.

In sum, the literature firmly supports the co-administration of antiemetics with anesthesia as a best practice for PONV prevention. Multimodal protocols leveraging the complementary mechanisms of agents like propofol, ondansetron, and dexamethasone provide the most robust protection, enhancing patient comfort and recovery outcomes.

#### 4. Results

The aggregated data from numerous randomized controlled trials, meta-analyses, and observational studies consistently demonstrate that co-administration of antiemetics with anesthesia significantly reduces the incidence and severity of postoperative nausea and vomiting.

For instance, a landmark meta-analysis encompassing over 4,000 patients found that ondansetron reduced PONV risk by 26%, dexamethasone by a similar margin, and propofol-based anesthesia lowered the risk by approximately 19%. When combined in multimodal protocols

these effects were additive, resulting in up to 50% or greater reduction in PONV incidence.

Clinical case studies reinforce these findings. A bariatric surgery program that implemented a standardized multimodal antiemetic and anesthesia protocol—including propofol infusions, ondansetron, and dexamethasone—reported a 40% reduction in reported nausea, a 35% decrease in vomiting episodes, and a significant decline in the use of rescue antiemetics. Patients also experienced shorter postoperative stays and reduced opioid consumption, highlighting broader benefits beyond PONV control.

Timing of antiemetic administration emerged as a critical factor. Studies showed that ondansetron given 15 minutes before surgical incision better occupied 5-HT<sub>3</sub> receptors, enhancing prophylactic effectiveness compared to later dosing. Similarly, dexamethasone's efficacy was maximized when administered early in the anesthesia course.

Adverse effects related to antiemetic co-administration were generally mild and infrequent. Headaches, dizziness, and transient QT interval prolongation were the most commonly reported, with no significant increase in serious complications documented.

Collectively, these results affirm that integrating antiemetic drugs with anesthetic management is an effective, safe, and clinically beneficial strategy to combat PONV.

#### 5. Discussion

The findings from this comprehensive review underscore the critical role of antiemetic co-administration with anesthesia in mitigating the burden of postoperative nausea and vomiting (PONV), a complication that significantly affects patient recovery and satisfaction. The integration of antiemetic drugs with anesthetic regimens, particularly those involving propofol, represents a paradigm shift from monotherapy approaches toward multimodal prophylaxis tailored to the complex neurochemical pathways underlying PONV.

Propofol's intrinsic antiemetic properties are particularly noteworthy. Unlike volatile agents that stimulate emetic centers, propofol exerts inhibitory-

effects on neurotransmitter release and receptor activation in the chemoreceptor trigger zone. This dual role as both a hypnotic and an antiemetic agent highlights the importance of anesthetic choice as a modifiable risk factor for PONV. The evidence reviewed confirms that total intravenous anesthesia (TIVA) using propofol consistently yields lower PONV incidence compared to inhalational anesthesia, supporting its preferential use in patients at elevated risk.

The synergistic effect observed with the concurrent administration of pharmacologic antiemetics targeting distinct receptor systems—serotonergic, dopaminergic, and corticosteroid-mediated—further amplifies prophylactic efficacy. The combination of ondansetron and dexamethasone exemplifies this synergy, producing additive reductions in PONV risk that exceed the effects of either agent alone. This supports current clinical guidelines advocating for multimodal antiemetic regimens, especially in patients with multiple predisposing factors.

However, the implementation of such protocols must be balanced against potential adverse effects and economic considerations. While the reviewed studies generally report favorable safety profiles, rare but serious side effects such as QT interval prolongation with certain agents necessitate vigilant patient monitoring and judicious drug selection. Cost-effectiveness analyses suggest that upfront investment in multimodal prophylaxis is offset by reductions in rescue medication use, shortened hospital stays, and improved throughput in ambulatory surgery settings.

An important practical consideration highlighted in the literature is the timing of antiemetic administration. Evidence suggests that preemptive dosing—prior to surgical incision or early intraoperatively—optimizes receptor occupancy and effectiveness. This temporal dimension to pharmacologic prophylaxis should be incorporated into perioperative protocols to maximize benefits.

Despite robust evidence supporting antiemetic co-administration, challenges remain in standardizing clinical practice. Variability in institutional protocols, surgeon and anesthesiologist preferences, and patient heterogeneity contribute to inconsistent application. Risk stratification tools such as the Apfel score offer a valuable framework for personalized prophylaxis but require broader adoption and integration into electronic health records to facilitate real-time decision-making.

Emerging therapies and approaches, including neurokinin-1 receptor antagonists and personalized medicine informed by pharmacogenomic profiling, hold promise for further reducing PONV. Additionally, non-pharmacologic adjuncts, including acupressure, aromatherapy, and optimized hydration strategies, present complementary avenues for comprehensive care.

From a systems perspective, embedding multimodal antiemetic strategies within enhanced recovery after surgery (ERAS) protocols exemplifies how coordinated multidisciplinary efforts can improve patient outcomes. Such initiatives emphasize the importance of cross-disciplinary communication, education, and quality improvement measures in sustaining gains against PONV.

In conclusion, the co-administration of antiemetics with anesthesia represents a cornerstone of modern perioperative care. It addresses a complex, multifactorial clinical problem with evidence-based, patient-centered strategies that improve comfort, reduce complications, and enhance recovery. Continued research, education, and quality initiatives are essential to optimize implementation and realize the full potential of these approaches across diverse surgical populations.

## 6. Conclusion

Postoperative nausea and vomiting (PONV) represent a persistent and multifaceted challenge in perioperative care, with an incidence that continues to affect a substantial proportion of surgical patients despite advances in anesthetic and surgical techniques. This review has underscored the critical importance of antiemetic co-administration alongside anesthesia as a cornerstone strategy for reducing the incidence and severity of PONV, ultimately improving patient outcomes and satisfaction.

The accumulated evidence robustly demonstrates that multimodal prophylactic approaches—particularly those combining propofol-based anesthetic techniques with pharmacologic agents



such as 5-HT<sub>3</sub> receptor antagonists (ondansetron) and corticosteroids (dexamethasone)—offer the most effective protection against PONV. The synergistic effects derived from targeting multiple neurochemical pathways involved in emesis not only reduce the direct physiological burden of nausea and vomiting but also mitigate the downstream complications associated with these symptoms, such as dehydration, electrolyte imbalances, and wound disruption.

Beyond clinical efficacy, the integration of antiemetic co-administration into anesthesia protocols carries significant operational and economic implications. By reducing PONV-related complications and the consequent need for rescue therapies, healthcare institutions can achieve shorter post-anesthesia care unit (PACU) stays, faster patient discharges, and decreased unplanned hospital admissions. These improvements contribute to enhanced patient throughput and potential cost savings, which are especially pertinent in high-volume surgical centers and ambulatory care settings.

The success of these regimens, however, hinges on individualized patient assessment and the thoughtful application of evidence-based guidelines. Risk stratification tools such as the Apfel score facilitate tailored prophylaxis, ensuring that patients receive appropriately intensive antiemetic therapy based on their unique risk profiles while minimizing unnecessary exposure to medications and potential side effects. This precision medicine approach aligns with the broader trend in healthcare toward personalized, patient-centered care.

Implementation challenges remain, including variability in institutional practices, clinician preferences, and resource availability. Overcoming these barriers requires multidisciplinary collaboration, ongoing education, and quality improvement initiatives designed to embed multimodal antiemetic protocols into routine perioperative workflows. Enhanced Recovery After Surgery (ERAS) programs provide an ideal framework for such integration, emphasizing standardized pathways that optimize all aspects of patient care, including PONV prevention.

Looking toward the future, promising developments in pharmacogenomics may enable clinicians to predict individual patient responses to antiemetics more accurately, further refining prophylactic strategies. Novel antiemetic agents and delivery methods, as well as adjunctive non-pharmacologic interventions such as acupressure and aromatherapy, hold potential to broaden and deepen the armamentarium against PONV. Rigorous research into these emerging modalities will be crucial to validate their efficacy and safety.

In conclusion, the co-administration of antiemetics with anesthesia represents a paradigm shift in perioperative medicine—transforming the management of PONV from reactive treatment to proactive prevention. By embracing multimodal, individualized strategies supported by robust clinical evidence, healthcare providers can substantially reduce the burden of PONV, enhancing patient comfort, improving recovery trajectories, and advancing the overall quality and efficiency of surgical care. This integrated approach exemplifies the evolution of anesthetic and perioperative practice toward holistic, patient-centered outcomes.

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