TMTD Türk Multidisipliner Tıp Dergisi
TURKISH JOURNAL OF MULTIDISCIPLINARY MEDICINE

OpusVia Publisher

Review

Prevention of Postoperative Nausea and Vomiting Following General Anesthesia: An Evidence-Based Review of Pharmacological and Anesthetic Strategies

Taylan Karslı [1],*

[1] Department of Anesthesiology and Reanimation, Kartal Dr. Lütfi Kırdar City Hospital, Istanbul, Türkiye

Corresponding author: Taylan Karslı | E-mail: drtaylankarslı@gmail.com

Received: 05.10.2026 ◆ Accepted: 25.10.2026 ◆ Published: 15.11.2026

Cite this article as: Karslı T. Prevention of postoperative nausea and vomiting following general anesthesia: an evidence-based review of pharmacological and anesthetic strategies. Turk J Multidiscip Med. 2026;1(1):23-30

Abstract

Background: Postoperative nausea and vomiting (PONV) remains a frequent and distressing complication after general anesthesia.

Objective: To compare evidence on 5-HT3 receptor antagonists, dexamethasone, multimodal prophylaxis, and anesthetic techniques.

Methods: A focused evidence-based narrative synthesis of identifiable clinical guidelines, systematic reviews, and meta-analyses available through November 2026 was prepared. This is not a completed PRISMA systematic review: comprehensive database screening, duplicate removal, independent selection, and formal risk-of-bias appraisal have not been performed.

Results: A Cochrane network meta-analysis of 585 trials involving 97,516 participants reported high-certainty evidence for preventing postoperative vomiting with ondansetron (risk ratio [RR] 0.55, 95% confidence interval [CI] 0.51–0.60) and dexamethasone (RR 0.51, 95% CI 0.44–0.57), each compared with placebo. Combinations were generally more effective than single agents. A meta-analysis found lower PONV risk with propofol maintenance than inhalational anesthesia (RR 0.61, 95% CI 0.53–0.69).

Conclusions: Risk-informed multimodal prophylaxis, avoidance of emetogenic exposures when feasible, and appropriate rescue treatment are supported by convergent evidence. Results should not be interpreted as a new pooled analysis.

Keywords: postoperative nausea and vomiting; ondansetron; dexamethasone; multimodal prophylaxis; total intravenous anesthesia; evidence synthesis

TMTD Türk Multidisipliner Tıp Dergisi
TURKISH JOURNAL OF MULTIDISCIPLINARY MEDICINE
OpusVia Publisher

Introduction

PONV encompasses nausea, retching, or vomiting after surgery and anesthesia. It can delay oral intake, prolong post-anesthesia care, reduce patient satisfaction, and occasionally contribute to unplanned admission. The mechanisms are multifactorial and involve serotonergic, dopaminergic, histaminergic, muscarinic, and neurokinin pathways. Therefore, preventive strategies should address both patient-specific susceptibility and modifiable perioperative exposures. [1,2,5]

The simplified Apfel score identifies four commonly used adult predictors: female sex, non-smoking status, previous PONV or motion sickness, and anticipated postoperative opioid exposure. Although useful for stratification, it does not replace individualized clinical judgment. [5,6]

Materials and Methods

The objective is to critically compare antiemetic medications, combination prophylaxis, propofol-based total intravenous anesthesia (TIVA), and supportive perioperative measures for adults undergoing general anesthesia. This manuscript synthesizes identifiable high-level evidence rather than claiming to have performed a complete systematic search. Sources were identified through targeted public literature retrieval of PubMed-indexed records and guideline publications. No database hit counts, screening flow diagram, protocol registration, or pooled treatment effect generated by the present authors is claimed. A publication-ready systematic review would require reproducible searches of PubMed/MEDLINE and at least one additional bibliographic database, a dated search strategy, predefined PICO criteria, independent screening, risk-of-bias appraisal, and PRISMA reporting. [7]

Results

3.1. Pharmacological prophylaxis

Ondansetron, a 5-HT3 antagonist, is a well-established prophylactic option. Dexamethasone, a corticosteroid, provides an alternative mechanism and is often combined with a 5-HT3 antagonist. The large network meta-analysis reported RR 0.55 (95% CI 0.51–0.60) for ondansetron and RR 0.51 (95% CI 0.44–0.57) for dexamethasone versus placebo for vomiting within 24 hours. These are comparisons with placebo, not a head-to-head proof that dexamethasone is superior to ondansetron. [2]

Aprepitant, an NK1 receptor antagonist, had an RR of 0.26 (95% CI 0.18–0.38) versus placebo in the same evidence synthesis. Differences in populations, baseline risk, outcomes, and intervention timing limit simplistic ranking of individual drugs. [2]

3.2. Combination regimens

Combinations of agents acting on distinct receptors generally outperformed monotherapy in the Cochrane network meta-analysis. Ondansetron plus dexamethasone is a commonly used example, but the optimal regimen depends on baseline risk, contraindications, cost, and availability. Current consensus guidance favors multimodal prophylaxis, particularly when risk is elevated. [1–3]

3.3. Anesthetic technique and opioid exposure

Propofol-based TIVA reduces exposure to volatile anesthetics and is associated with less PONV. A published systematic review and meta-analysis reported RR 0.61 (95% CI 0.53–0.69) compared with inhalational maintenance. Opioid-sparing multimodal analgesia and appropriate regional techniques may further reduce emetogenic exposure, although their benefits depend on surgical context. [3,4]

3.4. Supportive measures

Adequate perioperative hydration is another modifiable consideration. An abridged Cochrane review of supplemental intravenous crystalloid reported a reduction in postoperative nausea (RR 0.62, 95% CI 0.51–0.75) and vomiting (RR 0.50, 95% CI 0.40–0.63) in the studied populations. These findings do not justify indiscriminate fluid loading, especially in patients with cardiovascular or renal vulnerability. [8]

Table 1. Key evidence sources and their contributions

Source	Design / scope	Main contribution
Gan et al., 2020 [1]	International consensus guideline	Risk assessment, prophylaxis, rescue
Weibel et al., 2021 [2]	Network meta-analysis; 585 RCTs	Comparative drug effectiveness
Gan et al., 2026 [3]	Fifth consensus executive summary	Updated PONV management framework
Propofol meta-analysis [4]	Systematic review and meta-analysis	TIVA vs inhalational anesthesia
Apfel et al., 1999 [5]	Risk-score validation	Four-factor adult prediction score
Crystalloid review [8]	Cochrane systematic review	Supplemental fluids and PONV

Table 2. Selected reported effect estimates (not pooled in this manuscript)

Intervention / comparison	Outcome	Reported RR (95% CI)	Source
Ondansetron vs placebo	Vomiting within 24 h	0.55 (0.51–0.60)	[2]
Dexamethasone vs placebo	Vomiting within 24 h	0.51 (0.44–0.57)	[2]

Aprepitant vs placebo	Vomiting within 24 h	0.26 (0.18–0.38)	[2]
Propofol vs inhalational maintenance	PONV	0.61 (0.53–0.69)	[4]
Supplemental IV crystalloid vs control	Postoperative nausea	0.62 (0.51–0.75)	[8]
Supplemental IV crystalloid vs control	Postoperative vomiting	0.50 (0.40–0.63)	[8]

Table 3. Practical comparison of preventive strategies

Strategy	Potential advantage	Considerations
Ondansetron	Established 5-HT3 blockade	QT risk, timing, individual contraindications
Dexamethasone	Distinct mechanism; combines with 5-HT3 agents	Glucose effects and patient-specific contraindications
Ondansetron + dexamethasone	Multimodal receptor coverage	Do not assume universally optimal for every risk group
Propofol TIVA	Reduced volatile-anesthetic exposure	Resources, monitoring, surgical suitability
Opioid-sparing analgesia	Reduces emetogenic opioid exposure	Analgesic adequacy and patient factors
Appropriate hydration	Potentially reduces PONV in selected cases	Avoid fluid overload

3.5. Pathophysiological basis of preventive strategies

Postoperative nausea and vomiting is not mediated by a single neural pathway. The vomiting reflex integrates input from the gastrointestinal tract, vestibular system, higher cortical centers, and the area postrema through brainstem networks. Serotonin (5-HT3), dopamine (D2), histamine (H1), muscarinic, and substance P/neurokinin-1 (NK1) signaling contribute to emetic responses. This neurochemical diversity provides the rationale for combining antiemetic agents with different mechanisms rather than escalating the dose of one drug alone [1,2].

Anesthetic and surgical exposures influence these pathways at different times. Volatile anesthetics contribute especially to early postoperative symptoms, whereas postoperative opioid exposure can extend the period of susceptibility. A prevention strategy therefore needs to address both the immediate post-anesthesia care unit (PACU) interval and symptoms occurring after discharge. Preventing vomiting alone is insufficient if clinically meaningful nausea remains untreated; future studies should report these outcomes separately [1].

3.6. Risk assessment and patient selection

The simplified Apfel score assigns one point each for female sex, non-smoking status, a history of PONV or motion sickness, and anticipated postoperative opioid administration. It is useful for identifying patients who may benefit from more intensive prophylaxis, but it is a population-derived prediction tool rather than an individualized guarantee. Clinical judgment remains necessary for patients with prior severe PONV, limited access to rescue treatment, or procedures where retching could be particularly harmful [1,5].

Risk modification should precede drug selection whenever feasible. Avoidance of volatile agents, minimization of perioperative opioids, regional analgesia, and multimodal non-opioid pain management can lower the baseline emetic burden. These measures are not substitutes for pharmacological prophylaxis in patients with multiple risk factors; they are complementary components of a broader perioperative plan [1].

Clinical protocols should record preoperative risk factors, the antiemetics administered, their timing, and the patient's subsequent response. Standardized documentation facilitates local quality improvement and can identify systematic underuse of prophylaxis. Nevertheless, routine institutional audits involving identifiable patient data may require ethics or governance review depending on local requirements.

3.7. Ondansetron and other 5-HT3 antagonists

Ondansetron is a widely used 5-HT3 receptor antagonist with a substantial randomized-trial evidence base. In the Cochrane network meta-analysis, ondansetron reduced postoperative vomiting compared with placebo (RR 0.55, 95% CI 0.51–0.60), with high certainty for this outcome [2]. This estimate applies to vomiting in the first 24 postoperative hours and should not be interpreted as the same magnitude of benefit for nausea, rescue medication use, or patient satisfaction.

Clinical selection among 5-HT3 antagonists should consider duration of action, local availability, cost, previous patient response, and safety

factors. For agents with QT-prolongation potential, relevant patient characteristics and concomitant medications warrant attention. The evidence supports the class as an important preventive option, but does not establish that any single 5-HT3 antagonist is universally preferable across all surgical populations [1,2].

3.8. Dexamethasone: benefits and cautions

Dexamethasone acts through a mechanism distinct from serotonin antagonism and is frequently used as part of combination prophylaxis. The network meta-analysis estimated an RR of 0.51 (95% CI 0.44–0.57) for postoperative vomiting compared with placebo [2]. Its complementary mechanism makes it a practical partner for a 5-HT3 antagonist, particularly when more than one prophylactic intervention is appropriate.

Clinical interpretation must distinguish the evidence for antiemetic efficacy from uncertainty about adverse outcomes in specific subgroups. Perioperative glucocorticoid exposure may raise concerns regarding blood glucose, especially in patients with diabetes. The choice to use dexamethasone should therefore be individualized, accounting for the overall perioperative risk profile and local clinical guidance. These considerations do not negate its established antiemetic effect but highlight the need for balanced prescribing [1,2].

3.9. Combination prophylaxis and escalation

The strongest practical implication of the large network meta-analysis is that combinations of antiemetics generally perform better than single-agent prophylaxis [2]. This finding is biologically plausible because different medications interrupt distinct emetic signaling pathways. Ondansetron plus dexamethasone is a common combination; alternative or additional agents may be considered according to risk, contraindications, availability, and expected duration of postoperative symptoms.

Escalation should not be reduced to adding drugs indiscriminately. More complex regimens may increase cost, interactions, and medication-administration errors. The objective is to select complementary agents for the patient's risk level while simultaneously reducing avoidable emetogenic exposures. Comparisons between regimens should ideally report absolute risk differences and numbers needed to treat, because a relative risk reduction may have different clinical importance in low-risk and high-risk patients.

The Cochrane review assessed 585 randomized trials involving 97,516 participants, including 44 single drugs and 51 drug combinations. Its conclusions are robust in scale but not free from limitations: only 27% of studies were judged at overall low risk of bias, and safety data were often less informative than efficacy outcomes [2]. Accordingly, treatment rankings should be interpreted alongside certainty of evidence rather than used as a rigid prescribing hierarchy.

3.10. NK1 antagonists and other pharmacological options

NK1 receptor antagonists inhibit substance P-mediated emetic signaling and can provide substantial protection against postoperative vomiting. In the network meta-analysis, aprepitant had an estimated RR of 0.26 (95% CI 0.18–0.38) versus placebo, with high certainty for the evaluated vomiting outcome [2]. This does not mean that aprepitant is automatically the first-line choice for every patient; drug cost, availability, interactions, and the balance of nausea versus vomiting outcomes remain relevant.

Other drug classes, including dopamine antagonists, may be useful in selected settings or as rescue therapy. The consensus guideline discusses pharmacological options across multiple receptor systems and recommends matching prophylaxis to individual risk and clinical context [1]. The available review evidence is less definitive for some adverse events and drug-specific harms, so decisions should not be based on efficacy rankings alone [2].

3.11. Anesthetic technique and opioid-sparing care

Propofol-based total intravenous anesthesia (TIVA) is a preventive strategy that targets the baseline risk associated with volatile anesthetics. It is particularly attractive when the anesthetic plan can be modified without compromising other clinical priorities. The fourth consensus guideline identifies volatile agents and postoperative opioids as important modifiable contributors to PONV and supports anesthetic strategies that reduce these exposures [1].

An opioid-sparing pathway can combine regional techniques, non-opioid analgesics, and appropriate local anesthetic methods. Effective pain management remains essential: untreated pain can impair recovery, whereas indiscriminate opioid administration can increase emetic risk. Thus, the objective is balanced analgesia rather than withholding indicated analgesic treatment.

The comparison between TIVA and inhalational anesthesia is influenced by surgical type, baseline risk, concurrent prophylactic drugs, and outcome timing. These potential effect modifiers should be considered when interpreting trials and meta-analyses; a technique-associated reduction in PONV should not be presented as evidence of superiority for all other perioperative outcomes.

3.12. Rescue treatment and postdischarge symptoms

Prophylaxis does not eliminate all postoperative nausea and vomiting. When symptoms occur despite preventive therapy, clinicians should assess reversible contributors such as pain, hypotension, dehydration, and ongoing opioid exposure while selecting rescue treatment. A rescue antiemetic from a different pharmacological class is generally preferable when the same class has recently been administered, subject to clinical circumstances and local protocols [1].

Postdischarge nausea and vomiting may be particularly disruptive after ambulatory surgery because patients have limited access to intravenous medication and direct clinical assessment. Discharge instructions should specify what to do if oral intake is impossible, vomiting persists, or symptoms are accompanied by warning signs. Studies restricted to PACU observations may underestimate the patient-experienced burden across the first postoperative day.

3.13. Outcomes and interpretation of comparative evidence

PONV research uses heterogeneous outcomes: any nausea, any vomiting, complete response without rescue medication, time to first emetic episode, severity scores, and patient satisfaction. These outcomes are related but not interchangeable. In particular, the relative risks reproduced in this review describe vomiting, not a composite endpoint, and should not be generalized to every outcome of interest [2].

Absolute benefits depend on baseline risk. For illustration only, an RR of 0.55 would correspond to an estimated reduction from 30% to 16.5% if the untreated event risk were 30%; at a 10% baseline risk, the corresponding estimate would be 5.5%. These are arithmetic examples, not newly observed study results. This distinction matters when balancing treatment intensity against cost and adverse-effect concerns.

Network meta-analysis combines direct and indirect comparisons, which expands the number of treatments that can be compared but requires assumptions of comparability across trial populations and designs. Treatment ranking alone cannot replace examination of effect estimates, confidence intervals, study quality, and clinical relevance.

Discussion

The most consistent finding across high-level evidence is that prevention should target multiple pathways rather than rely on one antiemetic for every patient. Weibel and colleagues found that drug combinations generally reduced vomiting more effectively than single drugs. This is biologically plausible because emesis is mediated by several receptor systems. However, the network meta-analysis also reported that only 27% of included trials were judged to have low overall risk of bias, making certainty appraisal essential when translating rankings into practice. [2]

The strong placebo-controlled effects of ondansetron and dexamethasone should not be interpreted as proof of equivalence, superiority, or a particular optimal dose for all procedures. Their complementary mechanisms support combined prophylaxis in patients with clinically relevant risk, while side effects and contraindications must be considered. Fifth-consensus guidance provides an updated framework for this individualized approach. [1–3]

Anesthesia maintenance is a separate preventive lever. The reduction associated with propofol-based TIVA indicates that baseline emetogenic exposure can be modified before adding medication. Nevertheless, the choice of anesthetic technique also depends on patient comorbidity, procedure, equipment, and clinical expertise. Opioid minimization and multimodal analgesia can support prevention, but must not compromise pain control. [3,4]

The Apfel score remains useful because it translates readily identifiable factors into a structured preoperative assessment. Importantly, risk prediction is imperfect and published applications differ in how predictors are operationalized. An approach that combines assessment with broadly appropriate multimodal prophylaxis may therefore be more robust than rigid reliance on a score threshold alone. [5,6]

Fluid supplementation has demonstrated favorable effects in ambulatory or short-stay surgical populations, but its role is supportive rather than a substitute for antiemetic medication. The effect estimates come from a separate evidence base and should not be compared numerically as if all interventions were evaluated in a single randomized population. [8]

4.1. Implications for clinical protocols and future research

An effective institutional pathway can begin with structured risk assessment, continue with reduction of modifiable anesthetic risk factors, and provide multimodal prophylaxis for patients who are likely to benefit. Standardized rescue pathways and postdischarge guidance should complement the preventive plan. Protocol implementation should be evaluated using patient-centered endpoints, including nausea severity, vomiting episodes, rescue medication, recovery-room duration, and unplanned contacts after discharge [1].

Future comparative studies should distinguish early from delayed PONV, report nausea and vomiting separately, and capture adverse events with sufficient follow-up. Pragmatic trials could assess whether risk-adapted combination prophylaxis improves patient-reported recovery compared with a standardized multimodal approach. Cost-effectiveness research would also help clarify when newer agents add sufficient value to justify routine use.

Overall, the available evidence favors prevention through complementary pharmacological mechanisms and anesthetic risk reduction rather than reliance on a single antiemetic. However, the strength of the recommendation varies by intervention and outcome, and any clinical protocol should remain adaptable to local resources and individual patient characteristics.

Limitations

This manuscript is a targeted evidence-based review, not a completed systematic review. It has no preregistered protocol, exhaustive reproducible database search, formal duplicate screening, study-level

risk-of-bias assessment, PRISMA flow diagram, or original meta-analysis. Several cited sources are guidelines or secondary evidence syntheses, so overlap among their underlying randomized trials is possible. Outcomes and comparator groups differ between sources. These limitations preclude claims of comprehensive coverage or independently calculated comparative efficacy. [7]

Conclusion

For adults receiving general anesthesia, evidence supports risk-informed prevention of PONV using antiemetics with complementary mechanisms, propofol-based TIVA when appropriate, opioid-sparing analgesia, and individualized supportive measures. Ondansetron and dexamethasone each demonstrate efficacy against placebo; combinations generally provide stronger protection than monotherapy. A fully systematic review would require completion and documentation of PRISMA-compliant methods before journal submission under that article type.

Patents

Not applicable. No patents have resulted from the work reported in this manuscript.

Supplementary Materials

No supplementary materials are associated with this article.

Ethics

Not applicable. This evidence-based narrative review was conducted using previously published scientific literature and publicly available bibliographic information. No original research involving human participants, animals, or identifiable patient data was performed.

Author Contributions

Taylan Karslı: Conceptualization, methodology, investigation, literature review, formal analysis, data curation, writing—original draft preparation, and writing—review and editing. The author has read and approved the final version of the manuscript.

Funding

Funding information was not specified in the submitted manuscript.

Institutional Review Board Statement

Not applicable. This study is an evidence-based narrative review of previously published clinical guidelines, systematic reviews, and meta-analyses. No new clinical investigations, interventions involving human participants, animal experiments, or collection of identifiable patient information were conducted. Therefore, institutional ethics committee approval was not required.

Informed Consent Statement

Not applicable. This review did not involve the recruitment of human participants, collection of individual patient data, or publication of identifiable patient information.

Data Availability Statement

No new datasets were generated or analyzed in this study. The findings presented in this review are based on previously published clinical guidelines, systematic reviews, meta-analyses, and other scientific publications cited in the reference list. All reported comparative effectiveness estimates were obtained from the original published sources. No independent pooled analysis or individual participant-level data analysis was performed. The underlying evidence is available through the respective publications and their associated repositories, where applicable.

Acknowledgments

No acknowledgments were specified in the submitted manuscript.

Conflicts of Interest

The author's conflict-of-interest declaration was not provided in the submitted manuscript.

Abbreviations

The following abbreviations are used in this manuscript:

Abbreviation	Full Term
PONV	Postoperative Nausea and Vomiting
PDNV	Postdischarge Nausea and Vomiting
TIVA	Total Intravenous Anesthesia
5-HT3	5-Hydroxytryptamine Type 3 Receptor
NK1	Neurokinin-1 Receptor
RR	Risk Ratio
CI	Confidence Interval
RCT	Randomized Controlled Trial
PACU	Post-Anesthesia Care Unit
PICO	Population, Intervention, Comparison, Outcome
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
IV	Intravenous
QT	QT Interval

References

1. Gan TJ, Belani KG, Bergese S, et al. Fourth Consensus Guidelines for the Management of Postoperative Nausea and Vomiting. Anesth Analg. 2020;131(2):411–448. doi:10.1213/ANE.0000000000004833.

2. Weibel S, Schaefer MS, Raj D, et al. Drugs for preventing postoperative nausea and vomiting in adults after general anaesthesia: an abridged Cochrane network meta-analysis. Anaesthesia. 2021;76(7):962–973. doi:10.1111/anae.15295.

3. Gan TJ, Jin Z, Ayad S, et al. Fifth Consensus Guidelines for the Management of Postoperative Nausea and Vomiting: Executive Summary. Anesth Analg. 2026;143(3):497–513. doi:10.1213/ANE.0000000000007816.

4. Propofol vs. inhalational agents to maintain general anaesthesia in ambulatory and in-patient surgery: a systematic review and meta-analysis. PubMed PMID:30409186. https://pubmed.ncbi.nlm.nih.gov/30409186

5. Apfel CC, Läärä E, Koivuranta M, Greim CA, Roewer N. A simplified risk score for predicting postoperative nausea and vomiting: conclusions from cross-validations between two centers. Anesthesiology. 1999;91(3):693–700. doi:10.1097/00000542-199909000-00022.

6. Interpretation of the four risk factors for postoperative nausea and vomiting in the Apfel simplified risk score: an analysis of published studies. PubMed PMID:33721198. https://pubmed.ncbi.nlm.nih.gov/33721198ü

7. Page MJ, McKenzie JE, Bossuyt PM, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ. 2021;372:n71. doi:10.1136/bmj.n71.

8. Supplemental peri-operative intravenous crystalloids for postoperative nausea and vomiting: an abridged Cochrane systematic review. PubMed PMID:31536172. https://pubmed.ncbi.nlm.nih.gov/31536172