

# Postoperative Nausea and Vomiting Management, New Drugs in the Outpatient Setting



Aryana Valedon, BA, Anthony Tanella, MD, Jaime B. Hyman, MD\*

## KEYWORDS

- Postoperative nausea and vomiting (PONV)
- Postdischarge nausea and vomiting (PDNV) • Antiemetic • Outpatient • Ambulatory

## KEY POINTS

- Risk factors for postoperative nausea and vomiting (PONV) include female sex, nonsmoking status, prior PONV or motion sickness, opioids, and longer surgery.
- PONV can be measured using a nausea severity or impact scale and is included in patient-reported tools such as the Quality of Recovery 15.
- Combine antiemetics from different classes, give adequate intravenous fluids, avoid volatile anesthesia, and minimize opioids.
- Develop a plan for prevention and treatment of postdischarge nausea and vomiting for high-risk patients.

## INTRODUCTION

Postoperative nausea and vomiting (PONV) and postdischarge nausea and vomiting (PDNV) remain common, yet largely preventable, complications of surgery and anesthesia. Despite advances in anesthetic techniques and prophylactic strategies, nearly 30% of surgical patients experience these symptoms.<sup>1</sup> Importantly, patients rank PONV among the most distressing and undesirable postoperative outcomes. In one study, patients interviewed prior to surgery under general anesthesia were asked to rate the relative importance of 4 factors with regards to their recovery: alertness, pain, PONV, and additional costs. The relative importance of the 4 factors was found to be PONV (49%), pain (27%), alertness (13%), and additional costs (11%).<sup>2</sup>

Definitions vary slightly in the literature, but PONV is generally defined as nausea, retching, or vomiting occurring within the first 24 hours after surgery, while PDNV refers to symptoms occurring exclusively after discharge from the postanesthetic care unit (PACU).

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Department of Anesthesiology, Yale School of Medicine, 333 Cedar Street, TMP-3, New Haven, CT 06510, USA

\* Corresponding author.

E-mail address: [Jaime.hyman@yale.edu](mailto:Jaime.hyman@yale.edu)

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Abbreviations	
5-HT <sub>3</sub>	5-hydroxytryptamine type 3
AI	artificial intelligence
CNS	central nervous system
CTZ	chemoreceptor trigger zone
CYP3A4	Cytochrome P450 3A4
EMRs	electronic medical records
GI	Gastrointestinal
IV	intravenous
NK-1	neurokinin 1
NRS	numeric rating scale
NTS	nucleus tractus solitarius
ODT	oral disintegrating tablets
PACU	postanesthetic care unit
PBN	parabrachial nucleus
PDNV	postdischarge nausea and vomiting
PONV	postoperative nausea and vomiting
QoR-15	Quality of Recovery-15
StEP	Standardized Endpoints in Perioperative Medicine

Over the past several decades, surgical care has shifted from inpatient hospital settings to outpatient ambulatory surgery centers and office-based practices.<sup>3,4</sup> As this trend accelerates,<sup>5</sup> the clinical and economic impact of PONV and PDNV will become increasingly significant. These complications not only affect patient safety and satisfaction but also impose measurable costs on health care systems.

The economic considerations for surgical care must include the beginning of operating room time to discharge from the PACU. Patients who develop PONV typically remain in the PACU approximately 1 hour longer than those without symptoms.<sup>6</sup> This prolongation increases demands on PACU nursing staff, reduces throughput and operating room efficiency, negatively affects patient-reported quality of recovery, and increases costs by an estimated US\$75 per patient.<sup>6</sup> In contrast, the cost of appropriate prophylaxis is modest when compared with the resource utilization and downstream burden associated with PONV/PDNV.

In ambulatory surgery, particular attention must be given to long-acting prophylactic strategies, especially for patients at elevated risk of PDNV. Recent advances include extended duration antiemetics, combination regimens, and the application of machine learning and artificial intelligence (AI) to refine risk stratification and improve the precision of prophylaxis.<sup>7</sup> These innovations have the potential to further reduce the incidence, burden, and cost of PONV and PDNV in modern surgical care.

## **PATHOPHYSIOLOGY OF POSTOPERATIVE NAUSEA AND VOMITING AND POSTDISCHARGE NAUSEA AND VOMITING**

The pathophysiological mechanisms of PONV and PDNV have been extensively studied and have proven to be complex. The hypothesis that both nausea and vomiting are triggered via a common pathway has not been conclusively proven, and the mechanisms for each are distinct.<sup>8,9</sup> Both animal and human studies have helped elucidate the physiologic mechanisms triggering PONV and PDNV, as well as risk mitigation and treatment strategies.

Emesis may be preceded by nausea, an uncomfortable feeling caused by decreased gastric motility and increased intestinal parasympathetic tone<sup>10</sup> or retching, spasmodic respiratory movements with a closed glottis.<sup>11</sup> The mechanisms leading to emesis involve both central and peripheral neural pathways, which have converging

effects on the vomiting center, also known as the central pattern generator.<sup>12</sup> An emetic event involves a sequence of glottic closure, soft palate elevation, and the creation of negative intrathoracic pressure by diaphragm contraction. Such contraction helps open the esophageal sphincter and is followed simultaneously by forceful contraction of the abdominal wall muscles, which in turn leads to elevated intragastric pressure and expulsion of contents.

The vomiting center does not regulate nausea or retching, although they may share some common sensory pathways.<sup>8,13</sup> The parabrachial nucleus (PBN) has been identified as a primary relay in generating the subjective feeling of nausea and its affective responses. The PBN receives signals from the nucleus tractus solitarius (NTS) and vestibular system, and relays them to the amygdala, forebrain regions, hypothalamus, insular cortex, and limbic system, resulting in nausea (Fig. 1).<sup>8</sup>

The vomiting center is located bilaterally in the lateral medullary reticular formation at the level of the dorsal nucleus of the vagus nerve.<sup>14</sup> It receives afferent signals from 3 primary sources: the NTS, higher cortical centers, and chemoreceptor trigger zone (CTZ) in the area postrema (Fig. 2).

The NTS has receptors for dopamine (D2), substance P (neurokinin 1 [NK1]), serotonin (5-HT3), histamine (H1), and acetylcholine (M1). The NTS also receives signals from the vestibular system, which involves histamine (H1) and acetylcholine (M1), and vagal afferents from the gastrointestinal tract, which involves serotonin (5-hydroxytryptamine type 3 [5-HT3]). The higher cortical centers are involved in sensory input as well as sensations such as stress and anxiety. They can send emetic signals both directly to the vomiting center and indirectly via the NTS. Key neurotransmitters for these pathways include serotonin (5-HT3), dopamine (D2), histamine (H1), acetylcholine (M1), and substance P (NK1). The CTZ has mu opioid ( $\mu$ ), kappa opioid ( $\kappa$ ), dopamine (D2), substance P (NK1), and serotonin (5-HT3) receptors. The CTZ relays signals to the vomiting center via the NTS when its receptors detect emetic toxins in the blood or cerebrospinal fluid.<sup>15</sup> Receptors in the NTS, higher cortical centers, and CTS are targets of pharmaceuticals, some of which work best when used for prevention and others are more appropriate for rescue antiemetics (Table 1).

## RISK FACTORS

The Fourth Consensus Guidelines for the Management of Postoperative Nausea and Vomiting<sup>16</sup> represent the most current evidence-based recommendations for preventing and treating PONV and PDNV in both adult and pediatric populations. These guidelines were developed by an expert panel convened by the American Society for Enhanced Recovery, and they were endorsed by the Society for Ambulatory Anesthesia. The contributors conducted a comprehensive review of the literature up to September 2019, synthesizing clinical trials, meta-analyses, and practice-based evidence to provide practical, patient-centered recommendations. Key components include the identification of patient and procedure-specific risk factors, the use of multimodal prophylaxis, and strategies for postdischarge management. Risk stratification remains central to these guidelines, enabling clinicians to tailor prophylactic

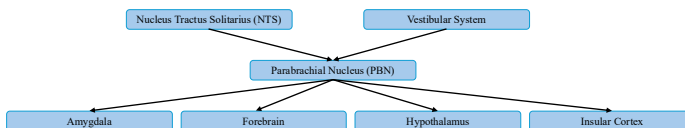


Fig. 1. Pathophysiology of nausea.

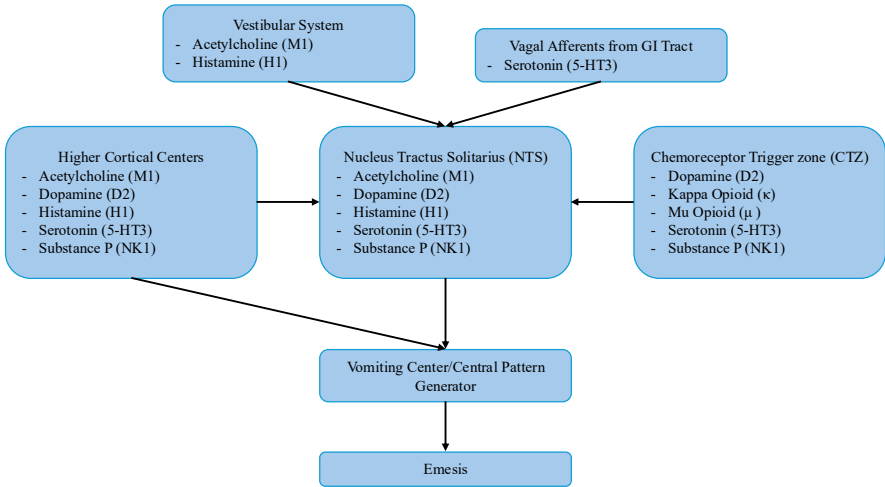


Fig. 2. Pathophysiology of emesis.

interventions to individual patients or procedure risk factors to minimize the incidence of PONV and PDNV (Table 2). Additionally, recent advances in machine learning and AI algorithms offer further risk stratification, helping to personalize prophylactic strategies beyond traditional guideline-based approaches.

While clinical risk factors remain the primary method for identifying at-risk patients, a substantial proportion of individuals continue to develop PONV despite appropriate assessment and prophylaxis, as a 70% reduction in the relative risk of PONV is the maximum that can be anticipated with total intravenous (IV) anesthesia plus 3 antiemetics

Neurotransmitter/ Receptor	Main Location(s)	Impacts PONV, PDNV, or Both	Role of Pharmaceuticals in this Pathway (Rescue, Prevention, and Both)
Serotonin/5-HT <sub>3</sub>	GI tract and brainstem (area postrema)	Both (w/longer acting agents)	Both
Dopamine/D <sub>2</sub>	CTZ and brainstem	Both (w/longer acting agents)	Both
Histamine/H <sub>1</sub>	Vestibular apparatus and CTZ	Mainly PONV	Both (less common for rescue)
Acetylcholine/M1	Vestibular apparatus, GI tract, and CTZ	Both	Prevention (occasionally rescue)
Substance P/NK-1	Area postrema, vagal afferents, and CNS	Both	Prevention (slow onset)
Opioid/μ	GI tract and brainstem	Both	Prevention (opioid-sparing)
Opioid/κ	GI tract and brainstem	Both	Prevention (opioid-sparing)

**Abbreviations:** 5-HT<sub>3</sub>, 5-hydroxytryptamine type 3; CNS, central nervous system; CTZ, chemoreceptor trigger zone; GI, gastrointestinal; M1, muscarinic type 1; NK-1, neurokinin 1; PDNV, postdischarge nausea and vomiting; PONV, postoperative nausea and vomiting.

Population	Model/Score	Risk Factors Included	Approximate Risk by Points
Adults—PONV	Apfel Score <sup>16</sup>	Female, nonsmoker, PONV/ motion sickness history, and postoperative opioids	0: ~10% 1: ~20% 2: ~40% 3: ~60% 4: ~80%
	Koivuranta Score <sup>17</sup>	Apfel predictors above + surgery >60 min	0: ~20% 1: ~20% 2: ~40% 3: ~50% 4: ~70% 5: ~90%
Adults—PDNV	Apfel-based Score <sup>16</sup>	Female, age <50 y, PONV history, PACU opioids, and PACU nausea	0: ~10% 1: ~20% 2: ~30% 3: ~50% 4: ~60% 5: ~80%
Children—POV	Eberhart <sup>16</sup>	Age >3 y, surgery >30 min, PONV/POV history (self or family), strabismus surgery	0: ~10% 1: ~10% 2: ~30% 3: ~50% 4: ~70%

*Abbreviations:* PACU, postanesthesia care unit; PDNV, postdischarge nausea and vomiting; PONV, postoperative nausea and vomiting; POV, postoperative vomiting.

from different classes.<sup>18</sup> This observation has prompted investigation into potential genetic contributions to susceptibility. Although several single nucleotide polymorphisms have been identified that may influence PONV,<sup>19,20</sup> current evidence suggests that the overall impact of genetic factors is less significant than that of established clinical risk factors.<sup>21</sup> Similarly, genetics also influence the pharmacokinetics and efficacy of antiemetic medications. For example, polymorphisms in the CYP2D6 enzyme system can accelerate the metabolism of drugs such as ondansetron and tropisetron, potentially reducing their effectiveness when prophylaxis or treatment is most needed.<sup>22</sup>

## MEASURING POSTOPERATIVE NAUSEA AND VOMITING/POSTDISCHARGE NAUSEA AND VOMITING

There are multiple approaches to measuring PONV. One commonly used endpoint is the administration of rescue antiemetic therapy.<sup>7,23–25</sup> While this measure is easily extractable from electronic medical records (EMRs), it is a clinician-initiated binary outcome that lacks granularity and may not reflect the full patient experience. Specifically, it can fail to capture subjective nausea that does not prompt intervention, thereby underestimating symptom burden. Furthermore, EMR-based documentation of rescue antiemetic use does not account for PDNV, which can significantly affect outpatient recovery.

Another commonly reported outcome is the incidence of vomiting defined as a binary variable (yes/no).<sup>26</sup> While this is a more objective measure than nausea, it disregards nausea severity, which may be more distressing to patients than actual emesis.

In contrast, nausea severity can be assessed using an 11 point numeric rating scale (NRS), ranging from 0 (no nausea) to 10 (worst imaginable nausea). This method provides greater sensitivity and captures a continuum of symptom severity, with scores greater than 3 generally considered indicative of moderate-to-severe nausea.<sup>27–29</sup> In addition, validated scoring systems such as the PONV Impact Scale developed by Myles and colleagues<sup>30</sup> can be used to quantify clinically important PONV. This scale includes 2 items: the number of vomiting or retching episodes and the degree to which PONV interfered with the patient's well-being or activities. Each item is scored from 0 to 3, yielding a total score of 0 to 6. A score of 5 or greater indicates clinically significant PONV, a threshold supported by the original validation studies and endorsed by the Standardized Endpoints in Perioperative Medicine (StEP) consensus guidelines,<sup>31</sup> which are described in more detail below.

Nevertheless, even mild PONV may negatively impact the patient experience. Broader, patient-centered instruments such as the Quality of Recovery-15 (QoR-15) capture the patient experience more comprehensively. The QoR-15 is a validated, patient-reported outcome measure that evaluates early postoperative recovery across 5 domains: physical comfort, emotional state, physical independence, psychological support, and pain.<sup>32</sup> Each of the 15 items is scored on an 11 point NRS (0–10), with total scores ranging from 0 to 150; higher scores indicate better recovery. Nausea and vomiting are included in the physical comfort domain, ensuring that their impact is reflected in the overall recovery profile.

The StEP initiative was established to address the considerable heterogeneity in how perioperative outcomes are defined and reported. In 2025, the group published an updated systematic review and consensus statement focused on endpoints related to patient comfort and pain relief.<sup>31</sup> Using a structured Delphi process (a method for gathering information and reaching consensus among a panel of experts through multiple rounds of anonymous questionnaires)<sup>33</sup> involving international experts, patients, and stakeholders, the group identified a core set of reliable, feasible, and patient-relevant outcome measures. For studies involving PONV, the group recommends inclusion of endpoints such as PONV at 0 to 6 hours, 6 to 24 hours, and overall, PDNV, severe PONV (PONV Impact Score >5), and the QoR-15.<sup>31</sup> The consensus statement emphasizes that at least some of these standardized, patient-centered outcomes should be incorporated into clinical trials and quality metrics evaluating patient comfort after surgery.

## PROPHYLACTIC AND THERAPEUTIC STRATEGIES

### *5-Hydroxytryptamine Type 3 Receptor Antagonists*

Ondansetron is the most extensively studied and widely used agent for PONV prophylaxis.<sup>26</sup> The elimination half-life of ondansetron is approximately 3 hours, and when administered intraoperatively, its clinical effect may not extend into the postdischarge period to prevent PDNV. To address this limitation, ondansetron oral disintegrating tablets (ODT) can be prescribed for use after discharge. In ambulatory laparoscopic gynecologic surgery, scheduled postdischarge administration of ondansetron ODT every 12 hours significantly reduced PDNV incidence.<sup>34,35</sup> However, a conflicting study in patients undergoing ambulatory laparoscopic surgery, predominantly laparoscopic cholecystectomy and laparoscopic fundoplication, found no benefit from postdischarge ondansetron ODT.<sup>36</sup>

Palonosetron, a second-generation 5-HT<sub>3</sub> receptor antagonist, has a markedly higher receptor affinity and an extended elimination half-life of approximately 40 hours. As monotherapy, it demonstrated superior effectiveness compared with a single 8 mg

dose of ondansetron in preventing PONV during the first 24 hours after ambulatory laparoscopic gynecologic surgery.<sup>37</sup> Another ambulatory trial evaluated palonosetron administered prior to PACU discharge and found no significant difference in the primary endpoint of complete response through postoperative day 2 compared with placebo.<sup>38</sup> In that study, most PDNV occurred on the day of surgery and rates were similar between groups; however, palonosetron significantly reduced PDNV on both postoperative day 1 and day 2. Overall, evidence suggests that a single dose of palonosetron provides effectiveness comparable to repeated doses of ondansetron for extended prophylaxis.<sup>39</sup>

### **Neurokinin-1 Receptor Antagonists**

Aprepitant is a NK-1 receptor antagonist available in both oral and IV formulations. A meta-analysis demonstrated that adding 80 mg of oral aprepitant to a standard prophylactic regimen of dexamethasone and ondansetron significantly reduced the risk of PONV, compared to dexamethasone and ondansetron alone, across a mix of ambulatory and inpatient populations.<sup>40</sup> Notably, aprepitant was more effective at preventing vomiting than nausea, and NK-1 receptor antagonists have been identified as the most effective class of antiemetics for vomiting prevention, with effectiveness comparable to that of many combination therapies.<sup>26</sup> This highlights their potential role in clinical scenarios where avoiding vomiting is of particular importance.

With a half-life of approximately 40 hours, aprepitant offers extended coverage that can span the postdischarge period after ambulatory surgery. Although studies specifically evaluating aprepitant for PDNV are limited, 1 trial in ambulatory plastic surgery patients compared aprepitant plus ondansetron to ondansetron alone, with outcomes measured through 48 hours. In that study, vomiting was rare in the aprepitant group and most vomiting episodes occurred after hospital discharge, underscoring its potential utility for PDNV prevention. However, the incidence of nausea was not significantly different between the 2 groups.<sup>41</sup> It is important to note that aprepitant can impact the effectiveness of hormonal contraception, and patients should be counseled to use barrier contraception for up to 2 months following administration of aprepitant.<sup>42</sup>

### **Dopamine Receptor Antagonists**

First-generation antipsychotics such as droperidol and haloperidol have long been recommended for the prevention and treatment of PONV.<sup>16</sup> More recently, attention has shifted toward second-generation (atypical) antipsychotics. Amisulpride, a dopamine D2/D3 receptor antagonist, is Food and Drug Administration-approved in an IV formulation for both the prevention and treatment of PONV. It has demonstrated effectiveness when administered as 5 mg at induction as monotherapy<sup>43</sup> or in combination with dexamethasone or ondansetron,<sup>44</sup> and as a 10 mg dose in patients who received no prophylaxis<sup>45</sup> or experienced breakthrough symptoms following prophylaxis.<sup>46</sup> Across these 4 pivotal trials, the primary endpoint was “complete response” (defined as no nausea or vomiting in the 24 hours postoperatively) and amisulpride outperformed placebo by an absolute difference of 10% to 13%.

A retrospective cohort study of 816 ambulatory surgery patients who experienced PONV found that the introduction of amisulpride was associated with a 26 minute reduction in PACU length of stay.<sup>47</sup> Additionally, a pharmacokinetic study suggested that a single 10 mg rescue dose of IV amisulpride may continue to exert antiemetic effects into the postdischarge period after ambulatory surgery,<sup>48</sup> although this has yet to be confirmed in clinical outcome studies.

Olanzapine is another atypical antipsychotic that has gained interest for off-label use in the prevention of PONV and PDNV.<sup>29,49–53</sup> It has a broad receptor profile,

antagonizing dopamine (D1, D2, and D4), serotonin (5-HT2A, 5-HT2C, and 5-HT3), alpha-1 adrenergic, histamine (H1), and multiple muscarinic receptors, with a half-life of approximately 30 hours. As monotherapy, oral olanzapine 10 mg was not significantly different from a standard regimen of dexamethasone plus ondansetron for preventing PDNV in the first 24 hours after discharge from ambulatory surgery.<sup>51</sup> In a separate study comparing 5 mg oral olanzapine to 16 mg oral ondansetron prior to laparoscopic cholecystectomy, early postoperative outcomes (0–8 hours) were similar, but olanzapine was associated with significantly less nausea between 8 and 24 hours postoperatively.<sup>53</sup> When used as part of combination therapy, oral olanzapine 10 mg added to dexamethasone and ondansetron significantly reduced PDNV after ambulatory gynecologic and plastic surgery<sup>54</sup> and reduced PONV in patients undergoing inpatient oncologic surgery.<sup>52</sup> A 5 mg oral dose, when combined with dexamethasone and granisetron, also demonstrated benefit in preventing PONV following laparoscopic gynecologic procedures.<sup>50</sup>

### ***Histamine Receptor Antagonists***

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Histamine H1 receptor antagonists, including diphenhydramine, dimenhydrinate, and promethazine, have a long clinical history in the prevention of PONV and PDNV. Their antiemetic effects are mediated primarily through antagonism of H1 receptors in the CTZ and vestibular nuclei, with additional weak anticholinergic properties contributing to their efficacy.<sup>16</sup> Although these agents are commonly available over the counter for the treatment of motion sickness, their clinical utility in the perioperative setting is limited by adverse effects. Sedation, dry mouth, blurred vision, urinary retention, dizziness, and even delirium, particularly in elderly patients, can restrict their role as first-line therapy. Consequently, H1 antagonists are more frequently employed as second-line or rescue antiemetics rather than as part of routine prophylaxis in modern PONV management strategies.

### ***Combination Drug Therapy***

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Combination drug therapy, defined as the use of 2 or more antiemetic agents from different pharmacologic classes, represents the mainstay of PONV and PDNV prophylaxis. Compared with monotherapy, combination regimens consistently demonstrate superior efficacy in reducing the incidence of nausea, vomiting, and the need for rescue antiemetics. While NK-1 receptor antagonists, when used as single agents, may provide comparable effectiveness to combination therapy<sup>16,26</sup> in the prevention of vomiting, this class of medication demonstrates less consistent effectiveness in the prevention of the subjective feeling of nausea, and their high cost can limit widespread adoption.<sup>55</sup> Although adverse events associated with antiemetic therapy are generally rare, the overall quality of evidence regarding potential complications remains low, warranting caution when selecting specific agents, particularly in high-risk populations. A detailed overview of considerations for antiemetic administration is provided in [Table 3](#).

The most widely recommended combination regimen includes dexamethasone and a 5-HT3 receptor antagonist such as ondansetron. This pairing has been shown to significantly reduce the need for rescue therapy when compared with 5-HT3 antagonists alone.<sup>56,57</sup> Evidence suggests that dexamethasone plus ondansetron not only decreases PONV incidence during the first 24 hours but may also extend protection against the need for rescue therapy up to 72 hours postoperatively, without increasing the risk of complications.<sup>56</sup>

Concerns regarding perioperative dexamethasone use center on potential metabolic and infectious risks. Meta-analyses have demonstrated that dexamethasone may cause a small but statistically significant increase in serum glucose levels.

**Table 3**  
**Specific concerns and adverse effects of classes of antiemetics**

Drug Class	Examples	Key Adverse Events	Clinical Considerations
5-HT <sub>3</sub> receptor antagonists	Ondansetron, granisetron, and palonosetron	QT prolongation, arrhythmias; headache; constipation; dizziness; rare serotonin syndrome	Avoid high-dose ondansetron (>16 mg IV); caution in long QT or with other QT-prolonging drugs
Corticosteroids	Dexamethasone	Transient hyperglycemia; theoretic infection/wound healing risk; rarely insomnia/mood changes	Single perioperative dose generally safe; monitor glucose in diabetics
NK-1 receptor antagonists	Aprepitant and fosaprepitant	CYP3A4 drug interactions; fatigue; hiccups; dizziness; injection-site reactions (fosaprepitant)	Check drug interactions (midazolam, warfarin, and hormonal contraceptives); generally well tolerated
Dopamine antagonists	Amisulpride, droperidol, haloperidol, and metoclopramide	QT prolongation (droperidol/haloperidol); extrapyramidal symptoms (dystonia, akathisia); sedation; anxiety	Droperidol and haloperidol safe at low doses but monitor QT; metoclopramide limited by extrapyramidal symptoms with repeated/high dosing
Antihistamines/ Anticholinergics	Diphenhydramine, promethazine, dimenhydrinate, and scopolamine	Sedation; dry mouth; blurred vision; urinary retention; delirium/confusion (elderly); mydriasis if scopolamine contacts eye	Useful adjuncts; caution in elderly; scopolamine patch applied preop
Atypical antipsychotic	Olanzapine (emerging use)	Sedation (notable in PACU); orthostatic hypotension; dry mouth	Long duration of action and effective in multimodal prophylaxis

*Abbreviations:* 5-HT<sub>3</sub>, 5-hydroxytryptamine type 3; CYP3A4, Cytochrome P450 3A4; IV, intravenous; NK-1, neurokinin type 1; PACU, postanesthesia care unit.

However, the clinical significance of this finding remains uncertain. Importantly, studies evaluating surgical outcomes in both diabetic and nondiabetic populations have found no increase in rates of wound infection or other surgical complications when dexamethasone is administered perioperatively.<sup>58,59</sup>

Taken together, these findings support combination antiemetic therapy as the standard of care for patients at moderate-to-high risk of PONV. Among available regimens, dexamethasone combined with a 5-HT<sub>3</sub> antagonist remains the most widely recommended strategy, balancing effectiveness, safety, and cost relative to newer agents such as NK-1 antagonists.

### Nonpharmacologic Interventions

Apart from acupuncture,<sup>60</sup> nonpharmacologic interventions such as chewing gum and aromatherapy have not proven effective in the treatment of PONV or PDNV.<sup>61,62</sup> Studies of chewing gum are intriguing as chewing gum is inexpensive with few side effects. Chewing gum does reduce the incidence of postoperative ileus<sup>63</sup> following bowel surgery so it may be that larger studies are needed to determine if it is noninferior to pharmaceutical interventions.<sup>61,64</sup>

Preoperative or intraoperative hydration, defined as 10 to 30 mL/kg via IV crystalloid is generally safe and effective for preventing PONV.<sup>16,65</sup> Preoperative carbohydrate drinks have also been studied for their potential benefits on insulin resistance, patient satisfaction and PONV. “Carbohydrate loading,” as it is often termed, is defined as patients consuming carbohydrate-based drinks 2 hours before surgery (carbohydrate doses of 12.5–67 g). Studies have shown mixed results with carbohydrate loading on rates of PONV. In sum, IV hydration, oral hydration, and chewing gum may be considered as a part of an overall strategy of patient satisfaction.<sup>66,67</sup>

Pyridoxine, or vitamin B<sub>6</sub>, is an intriguing intervention gaining attention for PONV prophylaxis.<sup>68</sup> Pyridoxine gained notoriety as a treatment of nausea and vomiting during pregnancy. Since then, it has expanded to evaluation for safe use for PONV. The results so far are promising and warrant further investigation to evaluate for broader utility.<sup>69</sup>

### Strategies to Reduce the Risk of Postoperative Nausea and Vomiting/Postdischarge Nausea and Vomiting

The implementation of effective risk mitigation strategies is equally as important as risk stratification in the management of PONV and PDNV. Several modifiable perioperative factors can be addressed to reduce the overall incidence of nausea and vomiting (Fig. 3).

When feasible, regional anesthesia is preferred over general anesthesia,<sup>70</sup> as it reduces exposure to emetogenic anesthetic agents and minimizes the intraoperative and postoperative use of opioids, both of which are major contributors to PONV. For patients who require general anesthesia, avoidance of volatile anesthetics and

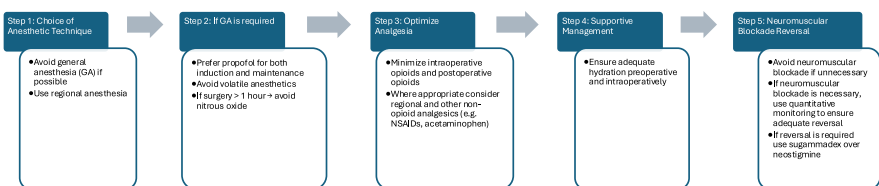


Fig. 3. Steps to minimize PONV before pharmacologic interventions.

nitrous oxide is recommended,<sup>18</sup> with propofol favored as both an induction and maintenance agent.<sup>71</sup>

Optimizing perioperative fluid management is another important strategy. Adequate preoperative hydration and intraoperative administration of crystalloids have been shown to decrease the risk of PONV, particularly in patients undergoing outpatient and laparoscopic procedures.<sup>65</sup>

Finally, neuromuscular blockade and its reversal should be carefully managed. If neuromuscular blockade is required, complete reversal must be ensured to avoid residual weakness and associated complications. When appropriate, sugammadex is preferred over neostigmine, as cholinergic agents have been associated with increased gastrointestinal side effects, which may exacerbate PONV.<sup>72</sup>

In summary, careful tailoring of the anesthetic plan to reduce reliance on emetogenic agents, minimize opioid use, optimize hydration, and appropriately manage neuromuscular blockade can significantly reduce the risk of PONV and PDNV.<sup>16</sup>

## SUMMARY

PONV and PDNV are common, undesirable, and costly complications of surgery and anesthesia that can prolong recovery and decrease patient satisfaction. Their pathophysiology involves complex central and peripheral pathways mediated by several neurotransmitters such as acetylcholine, dopamine, histamine, serotonin, and substance P. The receptors of these neurotransmitters are the targets of antiemetic pharmaceuticals. Accurate risk prediction is essential for tailoring prophylaxis and management. Key risk factors include female sex, nonsmoking status, history of PONV or motion sickness, opioid use, and duration and type of surgery. Multimodal prevention strategies that integrate pharmacologic and anesthetic approaches have proven to be most effective.

## CLINICS CARE POINTS

- *Risk factors:* Female sex, nonsmoking status, history of PONV or motion sickness, opioid exposure, longer surgeries, and certain procedures such as laparoscopic or strabismus surgeries increase risk of PONV and PDNV.
- *Measurement:* Assessing nausea using a 0 to 10 NRS, recording incidences of vomiting or retching, and patient-centered tools, such as the QoR-15, allow for more comprehensive insight into recovery and well-being.
- *Combination drug therapy:* Integrating antiemetics from different pharmacologic classes, such as dexamethasone combined with a 5-HT3 antagonist, is more effective than monotherapy.
- *Nonpharmacologic interventions:* Adequate preoperative and intraoperative hydration using IV crystalloids is effective for preventing PONV.
- *Anesthetic choice:* Using regional or propofol-based anesthesia and minimizing the use of volatile agents and opioids lowers the risk of PONV.
- *PDNV:* A plan for prevention and treatment of PDNV is essential for patients at high-risk.

## DECLARATION OF GENERATIVE ARTIFICIAL INTELLIGENCE AND ARTIFICIAL INTELLIGENCE-ASSISTED TECHNOLOGIES IN THE WRITING PROCESS

During the preparation of this article, the authors used ChatGPT to help improve readability and language of the work and not to replace key authoring tasks such as producing medical insights, drawing conclusions, or providing recommendations. After

using this tool, the authors reviewed and edited the content as needed and take full responsibility for the content of the published article.

## DISCLOSURE

The authors have nothing to disclose.

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