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# Postoperative and Postdischarge Nausea and Vomiting After Ambulatory Surgery: An Update

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**Abstract** Patients undergoing ambulatory surgery have similar, but also different nausea and vomiting stimuli and mechanisms than inpatients. As the emphasis on "street readiness" and discharge home is a unique and important concern for outpatients, various medications, formulations, techniques, risk scores, and guidelines have been introduced to help improve the care of patients having ambulatory surgery. Additional research and data have been obtained regarding the effects of postoperative nausea and vomiting (PONV) and postdischarge nausea and vomiting (PDNV) on ambulatory anesthesia. More effective antiemetic combination techniques and new long-acting antiemetics have been introduced for PONV and PDNV prevention. Antiemetic drug selection for ambulatory surgery depends on efficacy, cost, adverse effects, and ease of dosing. Safety concerns include adverse events such as the ECG QTc prolongation effects of antiemetics. To help guide antiemetic drug selection, techniques, and therapy, the PONV consensus guidelines were updated in 2014.

**Keywords** Antiemetics · Ambulatory anesthesia · Ambulatory surgery · Postoperative nausea and vomiting (PONV) · Postdischarge nausea and vomiting (PDNV) · Side effects

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## Introduction

Healthcare costs of ambulatory surgery related to postoperative nausea and vomiting (PONV) occur due to surgical complications, unanticipated hospital inpatient admissions, prolonged nursing care, and delayed discharge from the phase one post-anesthesia care unit (PACU) or phase 2 ambulatory care stepdown unit [1••]. PONV occurs with an overall average incidence of approximately 30 % taking into account all patient types and surgeries [1••]. Nausea occurs with an incidence of approximately 40–50 % and vomiting 25–30 % [1••, 2]. PONV incidence has been reported to be as high as 80 % in some high risk groups, such as patients who did not receive prophylactic antiemetics undergoing tonsillectomy, strabismus repair, or laparoscopy [3, 4].

Postdischarge nausea and vomiting (PDNV) is important in ambulatory patients discharged home and occurs with an incidence of about 30 % [5, 6]. The 2nd generation 5-hydroxytryptamine-3 ($5HT_3$) antagonist palonosetron (Aloxi®, Helsinn) [7] and the neurokinin-1 (NK-1) receptor antagonist aprepitant (Emend®, Merck) [8] both of which have long half-lives of 40 h, offer alternative therapy methods for the prophylaxis of PONV and PDNV in the ambulatory surgery patient. As dexamethasone and scopolamine patch have a prolonged duration of antiemetic effect, they are useful medications that can be used to help prevent PDNV.

The mechanisms and causes of PONV during ambulatory anesthesia are similar to those for inpatient surgery patients and are the result of anesthesia, surgical, and patient-related factors [9–11]. Anesthesia-related causes in the PACU are most commonly due to the intraoperative use of nitrous oxide and volatile anesthetics, as well as the postoperative use of oral and intravenous (IV) opioids [1••].

Many patients may or may not experience PONV due to their own individual PONV susceptibility and genetic makeup resulting in fast versus slow drug metabolism [9]. An important difference in the ambulatory surgery patient compared to inpatients is the impact of oral medications (especially opioids), early ambulation, and the advancement of food and liquids [1••, 12].

## Estimating the Risk of PONV and PDNV

Four risk factors that have been identified to contribute to PONV are: (a) female gender; (b) history of PONV and/or motion sickness; (c) non-smoker; and (d) postoperative opioids [13]. Each factor contributes a 20 % risk for PONV. The PONV risk factors are additive with a risk of 20, 40, 60, and 80 % for 1, 2, 3, and 4 risk factors, respectively. Four pediatric risk factors contributing to postoperative vomiting (POV) [14] are: (a) strabismus surgery; (b) age $\geq$3 years; (c) surgery >30 min; and (d) history of POV or postoperative nausea and vomiting in relatives (father, mother, siblings). These POV risk factors are additive risks of 10, 30, 50, and 70 % for 1, 2, 3, and 4 risk factors, respectively. In spite of receiving prior antiemetic prophylaxis, Apfel and colleagues [15•] identified the incidence of PDNV as 37 % in the first 48 h after hospital discharge. Five independent risk factors were found to cause PDNV: (a) female gender; (b) age less than 50 years; (c) history of nausea and vomiting after previous anesthesia; (d) PACU opioids; and (e) PACU nausea. The risk of PDNV was approximately 10, 20, 30, 50, 60, or 80 %, respectively, when 0, 1, 2, 3, 4, or 5 of these risk factors were present.

Apfel's "simplified" scores for PONV and PDNV have been used to estimate the degree of PONV and PDNV risk for ambulatory surgery patients. Improved cost-benefit and effective treatment measures occur in patients who have a PONV risk greater than 40 % (more than two Apfel PONV risk factors) [16••]. Use of simplified PONV and PDNV algorithms should allow for improved PONV prevention and treatment of ambulatory patients [17, 18]. Estimation of PONV and PDNV risk in the ambulatory patient population can help predict the chance of these patients having PONV and/or PDNV [14]. Use of risk scores can help predict which patients may have a low (10–20 %) or moderate to high risk (60–80 %) for PONV and PDNV [1••, 16••].

The "relatively" safe side-effect profile of the $5HT_3$ receptor antagonists and low cost of "generic" ondansetron has led to the practice by some anesthesia providers of giving antiemetics to all patients having ambulatory surgery. The real question is should one or two antiemetics with a low antiemetic side-effect profile be given universally to every ambulatory surgery patient in spite of these patients having a low PONV and/or PDNV risk? [19]. This approach of giving all patients antiemetic prophylaxis could cause low-risk patients to receive unneeded antiemetics and expose them to unnecessary risks for rare but possible side effects [1••]. However, most recent studies, including the 2014 PONV Consensus Guidelines indicate that routine use of 1–2 prophylactic antiemetics is beneficial with a superior risk : benefit ratio.

## Antiemetic Receptors and Their Antagonists

The etiology and mechanisms responsible for PONV and PDNV are similar and have been previously reviewed [11]. Numerous different neurochemicals and receptors are involved leading to the use of multimodal therapy to target these different receptor areas. A pertinent question for this review is does the mechanisms and types of antiemetic receptors for PONV and PDNV that occur in ambulatory outpatients differ from inpatients? In both types of patient populations, similar antiemetic receptor and pathways are involved, but the type and degree of antiemetic stimuli appear to be different [6, 20]. The cerebellum and vestibular areas relate to balance and movement, as occur when ambulatory patients increase their activity, ambulate, and begin their ride home from the hospital. The degree and amount of patient movement following discharge home from the hospital or ambulatory surgery center is an important difference between inpatients and outpatients. Nitrous oxide and the volatile anesthetics contribute to early but not delayed PONV after surgery [21]. Other stimuli to the chemoreceptor trigger zone and vomiting center are stimulation from opioids and movement via the vestibular part of the glossopharyngeal (8th cranial) nerve [1••, 10, 22].

## Pharmacogenetics

The human genome and genetic polymorphism influence an individual's pharmacogenetics, which in turn help determine which patients may or may not be affected by a specific drug therapy. Different genes in different patients control proteins activating specific receptors involved in the metabolism of a particular drug via liver enzymes. In turn, these genes can change an individual patient's response to a specific drug [9, 23]. Ultra-rapid metabolism results in lower blood levels with less drug effectiveness and increased antiemetic failure. Slower metabolism results in higher blood levels with possible drug toxicity [9, 23]. Ethnic genetic differences cause differences in enzyme metabolism due to genetic polymorphism [24]. The glycoprotein MDR1 is thought to affect drug metabolism and has genetic inter-individual variability [25].

**Table 1** Adult and pediatric antiemetic dosing for PONV and PDNV

| Type | Drug | Route | Dosing | Time of Admin. |
|---|---|---|---|---|
| Adults | | | | |
| Butyrophenones | Droperidol[a] | IV | 0.625–1.25 mg | End of surgery |
| | Haloperidol[a] | IV | 0.5-2 mg | Start or end of surgery |
| $5HT_3$ | Ondansetron[b] | PO | 8–16 mg | 1–2 h prior to start of Anesthesia |
| | | IV | 4 mg (prevention) | End of anesthesia |
| | | IV | 4 mg (treatment) | PACU |
| | Granisetron | IV | 0.25–1.0 mg (prevention) | Start of surgery |
| | Palonosetron | IV | 0.075 mg (prevention) | |
| NK-1 | Aprepitant | PO | 40 mg | 1–2 h prior to start of surgery |
| Steroids | Dexamethasone | IV | 2.5–4 mg | Start of surgery |
| | Methylprednisolone | IV | 40 mg | Start of surgery |
| Sedatives | Midazolam | IV | 2 mg | 30 min prior to end of surgery |
| Anti-cholinergic | Scopolamine | Transdermal | 1.5 mg patch | Prior evening or 2 hours prior to start of surgery |
| Pediatrics | | | | |
| Butyrophenones | Droperidol[a] | IV | 50–75 μg/kg up to 1.25 mg | End of surgery |
| $5HT_3$ antagonist | Ondansetron[b] | IV | 10 μg/kg up to 4 mg | End of surgery |
| | Granisetron | IV | 40 μg/kg up to 0.6 mg | End of surgery |
| Steroid | Dexamethasone | IV | 150 μg/kg up to 8 mg | Start of surgery |
| Antihistamine | Dimenhydrinate | IV | 0.5 mg/kg | End of surgery |

*IV* intravenous, *PO* per oral, *PACU* post anesthesia care unit, 5-$HT_3$ Serotonin (5-hydroxytryptamine3)

[a] US FDA black box warning

[b] Approved for postoperative vomiting in pediatric patients aged 1 month or older

## PONV Prophylaxis

The ambulatory surgery patient presents a special challenge compared to inpatients, as these patients usually will have less intense medical and nursing observation after discharge home. Safe "fast track" discharge home with "street readiness" is of utmost importance and once again raises the question whether prophylactic antiemetics should be given routinely to all ambulatory patients even though there is the possibility of rare but unwanted side effects. Some practitioners argue that liberal use of low risk antiemetics for PONV prophylaxis is a viable option to help totally eliminate or reduce PONV in the ambulatory patient population. However, one should remember that side effects of these medications, even if low, may be a possibility. The pressure to safely discharge patients home following ambulatory surgery requires a multimodal therapeutic prophylactic approach in patients at moderate (>40 %) to high (>60 %) risk for PONV [1••, 16••]. This is where the inclusion of one to two prophylactic antiemetics can be useful.

Eight antiemetics (ondansetron, dolasetron, granisetron, tropisetron, dexamethasone, droperidol, cyclizine, and metoclopramide) were evaluated by the Cochrane review [26••]. Each antiemetic was determined to reliably prevent nausea or vomiting after surgery. Interestingly, no drug was found to be especially better than another. When combined, their antiemetic effects were additive. Adult and pediatric antiemetic dosing are listed in Table 1.

### Metoclopramide

Metoclopramide is a weak antiemetic with a short half-life of 30 min to 1 h. Meta-analysis studies have determined that the 10 mg dose is ineffective and no better than placebo when given as PONV prophylaxis. Doses higher than 25 mg are needed for prophylactic PONV effectiveness, but extrapyramidal side effects occur at these higher doses. However, due to its prokinetic effects on the gastrointestinal system and increase of gastric emptying, metoclopramide is used by some clinicians as treatment for PONV post-surgery [1••, 27].

### Dexamethasone

Dexamethasone's minimum effective dose for PONV prophylaxis is 4 mg, with an increase in effectiveness occurring with an increase in dose [1••, 28]. The antiemetic mechanism of action of dexamethasone is not known, but is possibly related to its anti-inflammatory effect. As dexamethasone takes time to work, it should be given at the start of surgery. It is more effective preventing late versus early PONV. There

is increased effectiveness when dexamethasone is combined with other antiemetics [29, 30]. Controversy exists regarding the steroid side effects of postoperative wound and bone healing, bleeding, perineal pain, infection, and hyperglycemia [31–35]. Caution should be exercised in the use of dexamethasone in diabetic patients. With the availability of alternative antiemetics, an individualized review of the risks and benefits of using dexamethasome in these patients should be made [36, 37].

Methylprednisolone 40 mg IV has been shown to be effective to prevent late PONV occurring more than 6 h postoperative [38, 39]. Being also a steroid medication, methylprednisolone has characteristics similar to dexamethasone such as cortisol equivalency and side-effects profile.

### Transdermal Scopolamine

Because of its long duration of action given via the transdermal route, a useful antiemetic for ambulatory surgery and PDNV is transdermal scopolamine. Transdermal scopolamine has been found useful when used alone or in combination with other prophylactic antiemetics [40, 41]. Transderm scopolamine's main side effects are dry mouth and blurred vision occurring on the first and second postoperative days, respectively [42]. A transderm scopolamine patch contains a total 3-day dose of 1.5 mg with 0.5 mg used as the priming dose and a dose of 0.33 mg released per day over a 3-day period. Transderm scopolamine is FDA approved for 24 h for PONV and 72 h for motion sickness. Contraindications to transdermal scopolamine include acute angle glaucoma and voiding problems [1••, 42].

As blurred vision and pupillary changes can be a side effect of the scopolamine patch, it is the practice of this author to inquire with the operative surgeon if they have any concerns or questions about the use of the patch in their patients. This is important especially in neurosurgery or ENT surgery in which a change in vision (blurred) or pupil changes could indicate a CNS change or event. Also, a common question involves timing of patch placement. Current clinical practice is to apply the patch 1–2 h prior to surgery as this is the approximate time period in which patients may experience an increase in mouth dryness indicating that the patch is beginning to be absorbed from the skin to the blood stream. However, it is the opinion of this author that patch placement can also be made intraoperatively after anesthesia induction to have some effect for PDNV.

### Butyrophenones–Droperidol

Droperidol has been found to be more effective when given at the end of surgery [1••, 26••]. Droperidol has comparable effects against nausea and vomiting [43]. Droperidol doses of 0.625–1.25 mg IV have PONV efficacy equal to ondansetron [16••] and better effectiveness than metoclopramide [44]. It has been determined that, when given prophylactically at doses less than 1 mg (i.e., 0.625 mg) there was PONV efficacy with fewer side effects [45]. Following the FDA's 2001 "black box" QTc warning [46], droperidol was replaced by other antiemetics as the first choice for PONV prophylaxis in the USA and other countries. Combining droperidol with ondansetron does not cause any increased effects on QT prolongation [47].

### Haloperidol

Haloperidol, another medication in the butyrophenone drug class, has been suggested as an alternative antiemetic to droperidol but has a longer half-life. Haloperidol doses of 0.5 to 2 mg IV or intramuscular (IM) have been found to be effective in the prevention of PONV [1••]. Its administration at the start versus end of surgery showed no difference in PONV effect and equal efficacy compared to ondansetron [48–50]. When haloperidol was combined with other antiemetics it had a better effect compared to using one antiemetic alone [49]. Haloperidol has a similar effect on the QTc interval as droperidol, with similar QTc warnings issued by FDA in 2007 [48].

## $5HT_3$ Antagonists

### Ondansetron

Ondansetron is the "gold standard" antiemetic for PONV prophylaxis and treatment, with a recommended dose of 4 mg IV. It is effective when administered either at induction or end of surgery [1••]. However, because of a plasma half-life of 4–6 h, ondansetron dosing immediately prior to induction was less effective for prevention of PDNV compared to administration at the end of surgery [51]. Ondansetron is equally as effective as haloperidol [52], promethazine [53], and ramosetron [54], but less effective than palonosetron [55] and aprepitant [56]. Ondansetron 4 mg IV is equivalent to the 8 mg ondansetron oral disintegrating tablet (ODT). Because of its effect on the QTc interval, the FDA removed the ondansetron 32 mg dose for chemotherapy-induced nausea and vomiting from the US market [1••].

### Granisetron

Granisetron 0.35–3.0 mg IV has a similar antiemetic effectiveness compared to ondansetron, dolasetron and tropisetron [57, 58]. The combination of granisetron with another antiemetic is more effective than using only one antiemetic alone [59].

*Palonosetron- 2nd Generation $5HT_3$ Antagonist*

Palonosetron is a highly selective $5HT_3$ antagonist with a binding affinity stronger than the other 1st generation $5HT_3$ antagonists. It has a longer plasma half-life (40 h) than ondansetron, (4–6 h), dolasetron (7–9 h), granisetron (5–8 h), and tropisetron (7 h). Palonosetron has a chemical structure that is distinctly different from the 1st generation $5HT_3$ receptor antagonists. This structural difference allows palonosetron to have a unique and different molecular interaction with the $5HT_3$ receptor compared to 1st generation antagonists due to allosteric binding, positive cooperativity, and receptor internalization [60, 61]. Stronger binding and receptor internalization allow for easier attachment of subsequent palonosetron molecules after the first molecule attaches, resulting in a more prolonged inhibition of $5HT_3$ receptor function [61–63]. Due to its long half-life, the original early FDA new drug application studies chose to administer palonosetron at the start of surgery, similar to the new drug application for ondansetron. In an outpatient study, palonosetron 0.075 mg IV was the most effective dose for the 0- to 24-h postoperative time period [7]. Palonosetron 0.075 mg has greater PONV effectiveness compared to granisetron 1 mg [64] and ondansetron 4 mg [55]. Palonosetron is primarily metabolized by CYP2D6 and to a lesser extent by the CYP1A2 and CYP3A P450 liver enzymes. No dose adjustments are required regarding age, liver disease, or mild to moderate kidney disease. Palonosetron has no effect on the QTc interval [60, 62, 65].

Aprepitant-NK-1 Receptor Antagonist

Aprepitant is a NK-1 antagonist with a 40-h half-life that is given orally 1–2 h preoperatively for PONV prophylaxis. In a PONV prevention study, while ondansetron 4 mg IV and aprepitant 40 mg per oral (PO) had similar effectiveness for the first 24 h, aprepitant was more effective in the subsequent 24- to 48-h postoperative time period [8, 56] with an effect on vomiting greater than nausea. Aprepitant 80 mg PO was more effective than the 40 mg dose in patients undergoing laparoscopic gynecologic surgery. The combination of aprepitant plus dexamethasone was found to be more effective than ondansetron plus dexamethasone [66].

Midazolam

Midazolam's mechanism of action is believed to work by decreasing dopamine input at the chemoreceptor trigger zone and decreasing serotonin release at the GABA benzodiazepine complex [67]. Midazolam 2 mg IV given 30 min before the end of surgery decreased PONV more than midazolam 35 mcg/kg IV given as premedication [68]. Midazolam 2 mg was more effective than metoclopramide 10 mg [69] with similar PONV effectiveness compared to ondansetron 4 mg [70]. Given at the end of surgery, midazolam 2 mg IV was equally as effective as a 1 mg/kg/hr infusion of propofol [68]. Caution should be used with midazolam in the ambulatory patient as postoperative sedation is a possibility.

## Combination Antiemetic Therapy

Combination antiemetic therapy for PONV is more effective than giving a single drug alone [1••, 16••, 71, 72]. Drugs from different drug classes working at different antiemetic receptors should be combined to achieve the best effect. To decrease the incidence of side effects, the lowest effective dose of antiemetic should be used in the combination. The $5HT_3$ antagonists work best if they are used in combination with dexamethasone, transdermal scopolamine, or droperidol. However, because of additive side effects, the combined doses of these medications should not be more than ondansetron 4 mg, dexamethasone 10 mg or droperidol 1 mg [1••]. Examples of combination antiemetic therapy for PONV and PDNV are listed in Table 2.

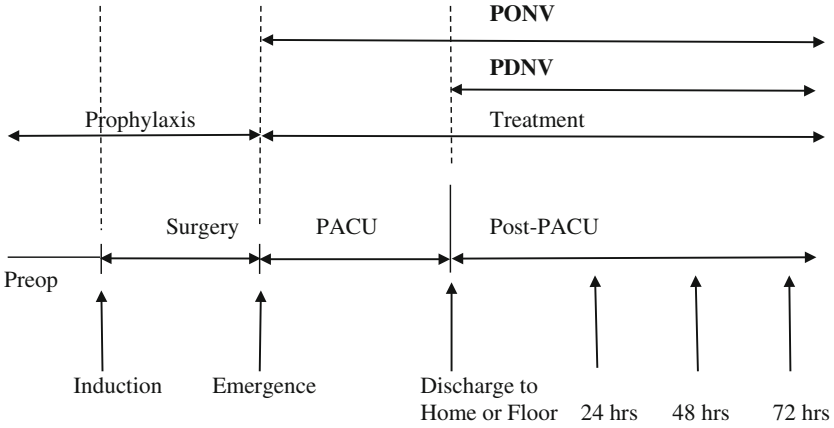
## Treatment of PONV

The 2014 PONV Consensus Guidelines [1••] recommend that for treatment of failed antiemetic prophylaxis, an antiemetic of a different drug class not previously administered should be given [73]. However, due to their

**Table 2** Combination antiemetic therapy for PONV and PDNV

| |
|---|
| PONV |
| a. Dexamethasone 10 mg IV at anesthesia induction + Ondansetron 4 mg IV at end of surgery |
| b. Scopolamine patch 1–2 h prior to surgery + Dexamethasome 5 mg IV at anesthesia induction ± Ondansetron 4 mg IV at end of surgery |
| PDNV |
| a. Dexamethasone 8 mg IV at anesthesia induction + Ondansetron 4 mg IV at end of surgery + Ondansetron 4 mg PO postoperatively at end of surgery |
| b. Dexamethasone 5 mg IV at anesthesia induction + Haloperidol 2.5 mg IV at end of surgery |
| c. Scopolamine patch 1–2 h prior to surgery + Dexamethasome 5 mg IV at anesthesia induction + Ondansetron 4 mg IV at end of surgery |

*PONV* postoperative nausea and vomiting, *PDNV* postdischarge nausea and vomiting, *IV* intravenous, *PO* per oral




PONV = Postoperative nausea and vomiting
PACU = Post-anesthesia care unit
PDNV = Post-discharge nausea and vomiting
Preop = Preoperative

**Fig. 1** Overlapping time periods of PONV and PDNV. Adapted from Kovac [78]

relatively short half-lives of less than 6 h, prophylactic-antiemetics from the same drug class given more than 6 h prior can be repeated. If no prior antiemetic was given for prophylaxis, a low-dose $5HT_3$ antagonist is recommended. Treatment of PONV has been shown to be effective with IV droperidol, promethazine, propofol, dexamethasone, or inhalation of isopropyl alcohol vapor. Treatment studies using long-acting antiemetics such as palonosetron, dexamethasone, aprepitant, or transderm scopolamine have not been conducted.

## Pediatrics

Tonsillectomy and strabismus repair are two of the most common outpatient emetogenic surgeries in children. Several prophylactic antiemetics have been found to be useful in pediatric patients. Ondansetron 0.1 mg/kg is effective to decrease POV in children 1 month to 2 years [74]. Children who received ondansetron oral disintegrating tabled (ODT) had less emesis and required less PACU rescue antiemetics [75, 76]. Combination antiemetics with dexamethasone have been determined to be effective in children [71, 77].

## Postdischarge Nausea and Vomiting (PDNV)

Multiple factors cause PDNV, and include the initiation of postoperative oral opioids, antibiotics, birth control pills, as well as increase in diet, movement, and ambulation. Some patients experiencing PDNV may not have received antiemetic prophylactic premedication or postoperative PONV treatment in the PACU. The perioperative time periods of PONV and PDNV overlap and are shown in Fig. 1 [78].

In outpatient surgery, PDNV occurs in approximately 30–40 % in patients who had or did not have PONV in the PACU [2, 5]. In a systematic review of PDNV in outpatient surgery patients, the nausea and vomiting incidence was 17 and 8 %, respectively [20]. Analysis of the simplified Apfel PDNV risk factors [15•] can help clinicians determine what patients may or may not have PDNV so that appropriate therapeutic measures can be undertaken [17, 79].

Additional prophylactic PO and IV antiemetics given at different times in the perioperative period may be necessary to prevent and/or treat patients for PDNV. Pan et al. [80•] determined that giving dexamethasone 8 mg IV at anesthesia induction, ondansetron 4 mg IV at the end of surgery and ondansetron 8 mg PO postoperatively was more effective to prevent PONV than giving ondansetron 8 mg IV alone at the end of surgery. A study [8] comparing the single prophylactic dosing of ondansetron 4 mg IV to aprepitant 40 mg PO determined that both drugs had similar effects on nausea and vomiting in the 0–24 h postoperative period, but for the 24–48 h postoperative period, aprepitant, with its longer 40 h half-life, had a greater antivomiting effect than ondansetron. When combining antiemetics for their effect on PDNV, haloperidol 2.5 mg IV plus dexamethasone 5 mg IV had more effectiveness than droperidol 1.25 mg IV, haloperidol 2 mg IV or dexamethasone 5 mg IV given alone [81]. Droperidol given at doses less than 1 mg (i.e., 0.625 mg) was found to be ineffective in preventing PDNV [82].

Possible useful approaches to help decrease the incidence of PDNV include: (a) combination prophylactic antiemetic therapy; (b) total intravenous anesthesia

(TIVA); substituting propofol for inhalation anesthesia; (c) P6 acupoint stimulation; and (d) use of long-acting antiemetics, such as dexamethasone, transdermal scopolamine, aprepitant, palonosetron, or ondansetron ODT [1••].

## Safety and Side Effects

The main side effects of antiemetics used for PONV and PDNV are sedation, hypotension, extrapyramidal and dystonic effects, restlessness, dry mouth, dysphoria, headache, lightheadedness, constipation, and ECG QTc prolongation [1••, 83–85]. See Table 3. Combining older antiemetics increases the likelihood of side effects. QTc prolongation is a side effect of droperidol, haloperidol, and the 1st generation $5HT_3$ receptor antagonists ondansetron, dolasetron and granisetron, but not the 2nd generation $5HT_3$ antagonist, palonosetron [65, 85, 86]. The newer antiemetics, such as palonosetron and aprepitant, do not have the side effects of the older antiemetics. Their own side effects include headache, constipation, and hunger [1••, 87–90].

**Table 3** Adverse Events of Currently Available Antiemetics

| |
|---|
| Dry mouth |
| Atropine |
| Scopolamine |
| Hydroxyzine |
| Antihistamines |
| Sedation |
| Phenothiazines |
| Antihistamines |
| Droperidol |
| Haloperidol |
| Hypotension |
| Promethazine |
| Prochlorperazine |
| Droperidol |
| Haloperidol |
| Dysphoria |
| Scopolamine |
| Droperidol |
| Haloperidol |
| Extrapyramidal symptoms |
| Benztropine |
| Metoclopramide |
| Droperidol |
| Haloperidol |
| Headache/lightheadedness, Constipation |
| Ondansetron |
| Granisetron |
| Tropisetron |
| Dolasetron |
| Palonosetron |
| Prolonged QTc interval |
| Ondansetron |
| Granisetron |
| Tropisetron |
| Dolasetron |
| Droperidol |
| Haloperidol |

During the trials of aprepitant for chemotherapy-induced nausea and vomiting (CINV), there was a clinical concern about the effect of aprepitant on female hormone levels as the efficacy of hormonal contraceptives, such as birth control pills, skin patches, implants, and IUDs, may be reduced during coadministration with and for 28 days after the administration of aprepitant. It was recommended that women should use a backup method of birth control during their treatment with aprepitant and up to 1 month after receiving aprepitant. The CINV dose of aprepitant is 125, 80, and 80 mg given on days one, two and three, respectively. The aprepitant PONV dose is a one time dose of 40 mg. While the hormonal effects of the CINV 125, 80, and 80 mg doses over 3 days have been studied, the hormonal effect of the reduced one time 40 mg PONV dose has not. As such, it is not known if these concerns for PONV are clinically relevant.

Metoclopramide administered in doses of 25–50 mg not only has prophylactic PONV effectiveness but also increased side effects of hypotension, tachycardia, and extrapyramidal symptoms [27]. Transderm scopolamine has side effects of dry mouth and blurred vision on the first and second postoperative days, respectively [42]. Case reports indicated the possible need for caution in children undergoing tonsillectomy due to an increased incidence of bleeding following dexamethasone [91–93]. In spite of this, ENT guidelines recommend the use of dexamethasone [94] and ondansetron [75] in tonsillectomy patients.

## Conclusions

PONV may occur in up to 80 % of high risk patients who do not receive prophylactic antiemetics. Overall, PONV and PDNV occur in about 30 % of patients. PONV and PDNV can occur in ambulatory surgery patients and are associated with increased morbidity and healthcare costs. Patient-specific, anesthesia-, and surgery-related PONV and PDNV risk factors should be evaluated to help determine the appropriate antiemetic therapy for proper prophylaxis or treatment. Volatile inhalation agents, opioids, early ambulation, and increases in fluids and diet are specific PONV and PDNV stimuli factors and triggers in the ambulatory surgery patient. Reducing a patient's risk for

PONV or PDNV can decrease the probability of these patients having nausea and/or vomiting after surgery. PONV antiemetic drug selection depends on efficacy, cost, safety, and ease of dosing. The 2014 PONV consensus guidelines are useful when applied to the ambulatory surgery patient to help determine proper antiemetic therapy and improve patient outcomes.

**Compliance with Ethics Guidelines**

**Conflict of Interest** Anthony L. Kovac has received grant support, participated on speaker's bureaus and served as an advisor for GlaxoSmithKline, Roche, Abbott, Merck, Baxter, Esiai, Hoechst Marion Roussel and Helsinn.

**Human and Animal Rights and Informed Consent** This article does not contain any studies with human or animal subjects performed by any of the authors.

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- • Of importance
- •• Of major importance


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