Consensus Guidelines for Managing Postoperative Nausea and Vomiting

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Postoperative nausea and vomiting (PONV) continues to be a common complication of surgery. It is a limiting factor in the early discharge of ambulatory surgery patients and is a leading cause of unanticipated hospital admission (1,2). PONV can lead to increased recovery room time, expanded nursing care, and potential hospital admission—all factors that may increase total health care costs. Equally important are the high levels of patient discomfort and dissatisfaction associated with PONV. Patients report that avoidance of PONV is of greater concern than avoidance of postoperative pain (3) and are willing to spend up to US$100 out of pocket for an effective antiemetic (4), yet more than a quarter of patients continue to experience PONV within 24 h of surgery (5,6). Among high-risk patients, the incidence of PONV can be as frequent as 70% to 80% (7). Published evidence suggests that universal PONV prophylaxis is not cost-effective. Although some advocate prophylactic antiemetic therapy for high-risk patients and rescue antiemetic treatment for episodes of PONV, the optimal approach to PONV management remains unclear to many clinicians. Guidelines for prevention and treatment of PONV based on data from systematic reviews of randomized trials have been published (8,9). However, these guidelines did not consider evidence from sources other than systematic reviews. Evidence from single studies or data from logistic regression (aiming to identify risk factors for PONV) were not included. These guidelines also need to be updated with new evidence on the control of PONV.

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Establishment of Expert Guidelines

A multidisciplinary panel of experts convened to review the medical literature on PONV (up to February 2002) and to produce guidelines for its management that were valid, reliable, clinically applicable, flexible, and clear. In establishing the guidelines, the panel based their recommendations on available evidence

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regarding the prevention or minimization of PONV with prophylactic and/or rescue therapy. Members of the panel were assigned specific topics to review before the meeting. Evidence was then presented and discussed at the meeting before a consensus was reached. When full agreement could not be obtained, the majority view was presented, and the lack of full agreement was stated.

Goals of Guidelines

The panel defined the following goals for the guidelines: 1) identify the primary risk factors for PONV in adults and children, 2) reduce the baseline risks for PONV, 3) identify the optimal approach to PONV prevention and therapy in various patient populations, 4) determine the optimal choice and timing of antiemetic administration, and 5) identify the most effective antiemetic monotherapy and combination therapy regimens.

Strength of Evidence

The panel consulted the medical literature for level of evidence rating scales that were pertinent and widely used and then adapted them to the body of scientific literature relating to PONV (10,11). In the absence of published data, recommendations were made on the basis of expert opinion. The scales used in rating the guidelines are shown in Table 1.

The aim of the evidence rating scale was to present information on both the design and the source of the data (I to V) independent of the validity of those data. The quality of the data was judged by the panel, which determined whether the recommendation was good, fair, or insufficient. For instance, a logistic regression analysis that aims to identify risk factors for PONV would be in Level IV, because such trials are not randomized. However, information emerging from that study may be judged as "A" by the panel.

Consensus Guidelines

The panel agreed that recommendations for PONV prophylaxis and treatment must consider the following factors: the patient's level of PONV risk; potential morbidity associated with PONV, including suture dehiscence (12), esophageal rupture (13,14), hematoma formation, and aspiration pneumonitis (15); potential adverse events associated with the various antiemetics, in particular the recent Food and Drug Administration (FDA) warning about QT prolongation and fatal arrhythmias associated with droperidol; efficacy of antiemetics; costs of antiemetic therapy; and increased health care costs associated with PONV.

Table 1. Evidence Rating Scale

Level of evidence based on study design
I Large randomized, controlled trial, $n \geq 100$ per group
II Systematic review
III Small randomized, controlled trial, $n < 100$ per group
IV Nonrandomized, controlled trial or case report
V Expert opinion
Strength of recommendation based on expert opinion
A Good evidence to support the recommendation
B Fair evidence to support the recommendation
C Insufficient evidence to recommend for or against

The panel agreed that not all patients should receive PONV prophylaxis. In general, patients at small risk for PONV are unlikely to benefit from prophylaxis and would be put at unnecessary risk from the potential side effects of antiemetics. Thus, prophylaxis should be reserved for those patients at moderate to high risk for PONV. In developing these guidelines, the panel deliberately chose, for several reasons, not to quantify the percentage of patients who would be in the low-, moderate-, and high-risk categories. The sensitivity and specificity of the various risk scoring systems are not 100% (only approximately 70%) and hence have a degree of uncertainty (16–18). Even if health care providers knew with confidence the true underlying risk, their and the patient's perception of this risk and, thus, the need for prophylaxis, would not be universally accepted. The decision was made, instead, to allow the health care professionals who use the guidelines to determine the level of risk according to their own local and institutional norms. For instance, although a 20% incidence of PONV may constitute a small risk in some institutions, it may be considered a moderate risk in others because of institutional variations in rates of ambulatory surgery, types of surgery, and patient populations. In addition, the decision to give antiemetic prophylaxis should be reached by both the care provider and the patient on the basis of the best available evidence.

Throughout the guidelines, antiemetic efficacy was expressed as number needed to treat (NNT) whenever this information was available from the literature. In this context, a NNT indicates the number of patients with a high baseline risk (corresponding to a control- or placebo-event rate of 40%–80% in a randomized, controlled trial) and who needed to receive a particular antiemetic intervention to prevent one emetic event that would have occurred had the patient not received the intervention (19). When a dose range is presented, the smallest dose is recommended. Risk of adverse drug reactions is expressed as number needed to harm whenever this information was available from the literature.

Table 2. Risk Factors for Postoperative Nausea and Vomiting (PONV) in Adults

Patient-specific risk factors (7,16,17)
Female sex (IA)
Nonsmoking status (IVA)
History of PONV/motion sickness (IVA)
Anesthetic risk factors
Use of volatile anesthetics within 0 to 2 h (IA) (20)
Nitrous oxide (IIA) (21)
Use of intraoperative (IIA) and postoperative (IVA) opioids (7,18,21–23)
Surgical risk factors
Duration of surgery (each 30-min increase in duration increases PONV risk by 60%, so that a baseline risk of 10% is increased by 16% after 30 min) (IVA) (16)
Type of surgery (laparoscopy, ear-nose-throat, neurosurgery, breast, strabismus, laparotomy, plastic surgery) (IVB) (16,24,25)

Guideline 1: Identify Adults at High Risk for PONV

Risk factors for PONV in adults are shown in Table 2. The identification of individuals at high risk for PONV can narrow the pool of potential candidates for prophylactic antiemetic therapy, indicating those most likely to benefit and reducing antiemetic side effects and costs for patients unlikely to benefit.

Apfel et al. (7) created a simplified risk factor chart identifying four primary risk factors for PONV in patients receiving balanced inhaled anesthesia: female sex, nonsmoking status, history of PONV, and opioid use. The incidence of PONV with the presence of none, one, two, three, or all four of these risk factors was approximately 10%, 20%, 40%, 60%, and 80%, respectively. This simplified risk score was recently validated in inpatients (18,26).

The panel did not reach full agreement about the association between type of surgery and increased PONV risk; thus, type of surgery was given a strength of evidence rating of B. Apfel et al. (7) found that type of surgery was not an independent risk factor for PONV. When other risk factors, such as type of anesthetic and duration of operation, were considered, a causal effect on PONV by type of operation could not be established in this study. The panel noted that these data were based on inpatient surgical cases. In addition to the above-mentioned risk factors by Apfel et al., a large study of 18,000 ambulatory patients showed an increased risk for PONV (>15%) among patients undergoing breast augmentation, dental surgery, orthopedic shoulder procedures, gynecologic laparoscopy (for sterilization), varicose vein stripping, and strabismus repair (16).

Guideline 2: Identify Children at High Risk for Postoperative Vomiting

Risk factors for postoperative vomiting (POV) in children are shown in Table 3. The panel recommended identification of children at high risk for POV as candidates for prophylactic antiemetic therapy. Because of the difficulty in diagnosing nausea in younger children, only vomiting is studied and treated in this population. POV is problematic in children. It is one of the leading postoperative complaints from parents and the leading cause of readmission (28).

Table 3. Risk Factors For Postoperative Vomiting (POV) in Children

Risk factors for children are similar to those in adults, with the following differences:
Studies in children are often limited to data on vomiting only and not nausea
Vomiting incidence is twice as frequent among children as among adults (5)
Risk increases as children age, decreasing after puberty
Sex differences are not seen before puberty (27)
Risk increases more consistently with specific operations (5)

Most risk factors for POV in children are the same as those in adults, with several important differences. POV increases as children age. It is rare in children younger than 2 yr old. However, children aged ≥3 yr have an average vomiting incidence of ≥40%—almost twice as frequent as the rate in adults (5). The increased vomiting incidence tapers when children reach puberty. Sex differences in risk of vomiting are not seen in children before puberty (27). Operations associated with an increased incidence of vomiting in children include adenotonsillectomy, strabismus repair, hernia repair, orchiopexy, and penile surgery (5).

Guideline 3: Reduce Baseline Risk Factors for PONV

Approaches for decreasing baseline risk factors are presented in Table 4. A reduction in baseline risk factors can significantly decrease the incidence of PONV (8,9). The panel thus recommended reducing baseline risk when clinically practical. Sinclair et al. (16) found that patients receiving general anesthesia had an 11-fold increased risk for PONV compared with those receiving regional anesthesia. Propofol, administered for the induction and maintenance of anesthesia, effectively reduced early PONV incidence (0–6 h) (29). The NNT with propofol to reduce PONV

Table 4. Strategies to Reduce Baseline Risk

Use of regional anesthesia (IIIA) (16)
Use of propofol for induction and maintenance of anesthesia (IA) (29)
Use of intraoperative supplemental oxygen (IIIB) (30,31)
Use of hydration (IIIA) (32)
Avoidance of nitrous oxide (IIA) (19,33)
Avoidance of volatile anesthetics (IA) (18,20)
Minimization of intraoperative (IIA) and postoperative (IVA) opioids (7,18,21–23)
Minimization of neostigmine (IIA) (34)

is approximately 5, compared with not using propofol. Among patients undergoing colon resection, use of supplemental oxygen (80% oxygen) reduced PONV by half when it was administered perioperatively and for 2 h after surgery (30). Oxygen supplementation restricted to the intraoperative period also halved the risk of PONV (31). Hydration reduced the incidence of PONV (32). Avoiding nitrous oxide and volatile inhaled anesthetics and minimizing intraoperative and postoperative opioid use reduced the incidence of PONV (7,18-23,33). To achieve satisfactory analgesia without opioids, alternate modalities of pain management may be used. For instance, in patients undergoing tonsillectomy, nonsteroidal antiinflammatory drugs (NSAIDs) and opioids are equianalgesic, but NSAIDS are less emetogenic; the NNT to prevent PONV with a NSAID during surgery compared with an opioid is approximately 9 (22). Neostigmine, used at the end of surgery, is associated with increased PONV, especially when used in large doses (>2.5 mg) (34). Minimizing large doses of this drug can reduce PONV. Many of the aforementioned strategies to reduce baseline PONV risk have been incorporated into a multimodal approach to minimize PONV (35). Scuderi et al. (36) tested the efficacy of a multimodal approach to reducing PONV. Their multimodal approach consisted of preoperative anxiolysis and aggressive hydration; oxygen; prophylactic antiemetics (droperidol and dexamethasone at the induction and ondansetron at the end of surgery); total IV anesthesia with propofol and remifentanil; and ketorolac. No nitrous oxide or neuromuscular blockade was used. Patients who received multimodal therapy had a 98% complete response rate, compared with a 76% response rate among patients receiving antiemetic monotherapy and a 59% response rate among those receiving routine anesthetic plus saline placebo.

Guideline 4: Antiemetic Therapy for PONV Prophylaxis in Adults

Prophylactic doses and timing for the administration of antiemetics in adults are shown in Table 5.

Serotonin Receptor Antagonists. The panel agreed that there is no evidence of any difference in the efficacy and safety profiles of the serotonin (5-HT_3) receptor antagonists—ondansetron, dolasetron, granisetron, and tropisetron—in the prophylaxis of PONV. These drugs are most effective when given at the end of surgery (38,39). Most research on the 5-HT_3 receptor antagonists has been performed with ondansetron, which has greater antivomiting than antinausea effects (37). Ondansetron 4 mg has a NNT of approximately 7 in the prevention of nausea compared with placebo (0–24 h); the 8-mg dose has a NNT of approximately 6 (37). For the prevention of vomiting (0–24 h), ondansetron 4 mg has a NNT of approximately 6; the 8-mg dose has a NNT of approximately 5 (37). Dolasetron has shown efficacy for the prophylaxis of PONV at a dose of 12.5 mg. In a study of 635 high-risk patients, Graczyk et al. (39) found a statistically significant increase in complete responders, a decreased need for rescue antiemetic, less nausea, and more patient satisfaction with dolasetron versus placebo. Granisetron 0.35–1 mg and tropisetron 5 mg are also used for PONV prophylaxis and treatment (40-43). Smaller doses of granisetron (0.1 mg) are effective when used for treatment (83). When a dose range is presented, the smallest dose is recommended. The 5-HT_3 antagonists have a favorable side effect profile and are considered equally safe. The number needed to harm with a single dose of ondansetron is 36 for headache, 31 for increased liver enzymes, and 23 for constipation; this means, for example, that 36 patients would need to be treated with a single dose of this drug for one to develop headache who would not have done so had they all received a placebo (37).

Dexamethasone. Dexamethasone, administered at a prophylactic dose of 8–10 mg IV, effectively prevents nausea and vomiting with a NNT of approximately 4 (44). More recently, smaller doses (2.5–5 mg) have been found to be as effective (45,46). Dexamethasone appears to be most effective when administered before the induction of anesthesia rather than at the end (47). Side effects with long-term administration of corticosteroids can include wound infection and adrenal suppression, among others, but adverse events have not been noted after a single bolus dose of dexamethasone (44).

Droperidol. Prophylactic doses of droperidol (well below 1 mg) are effective for the prevention of PONV (48–50). The efficacy of droperidol is equivalent to that of ondansetron for PONV prophylaxis, with a NNT of approximately 5 for prevention of nausea and vomiting (0–24 h) (8). Droperidol is most effective when administered at the end of surgery (50). It is also effective when given concomitantly with patient-controlled analgesia devices that deliver morphine, with a NNT of approximately 3 (57). Recently, the FDA issued a "black box" warning about droperidol (58). The warning states that droperidol may cause death or life-threatening events associated with QT prolongation and torsades de

Table 5. Antiemetic Doses and Timing for Administration in Adults

Drug	Dose	Evidence	Timing	Evidence
Ondansetron	4–8 mg IV (37)	IA	At end or surgery (38)	IIIA
Dolasetron	12.5 mg IV (39)	IA	At end of surgery (39)	IIIA
Granisetron	0.35–1 mg IV (40–42)	IA	At end of surgery (40,42)	IIIA
Tropisetron	5 mg IV (43)	IA	At end of surgery	VA
Dexamethasone	5–10 mg IV (44–46)	IIA	Before induction (47)	IIIA
Droperidol	0.625–1.25 mg IV (48,49)	IA	At end of surgery (50)	IIA
Dimenhydrinate	1–2 mg/kg IV (51)	IIA		
Ephedrine	0.5 mg/kg IM (52)	IIIB		
Prochlorperazine	5–10 mg IV (53)	IIIA	At end of surgery (53)	IIIB
Promethazine	12.5–25 mg IV (54)	IIIB	At end of surgery (54)	IIIB
Scopolamine	Transdermal patch (55,56)	IIB	Applied prior evening or 4 h before end of surgery (56)	IIB

When a dose range is presented, the smallest dose is recommended.

pointes. This warning is based on 10 reported cases (1.25 mg or below) in association with droperidol use over the approximately 30 yr that it has been available on the market (84). It is interesting to note that there has not been a single case report in a peer-reviewed journal in which droperidol in doses used for the management of PONV has been associated with QTc prolongation, arrhythmias, or cardiac arrest (35). Likewise, in Europe and elsewhere, there has been no such report. The panel expressed considerable concerns about the quality and quantity of evidence and the validity of the FDA conclusion. If it were not for the "black-box" warning, droperidol would have been the panel's overwhelming first choice for PONV prophylaxis.

Other Antiemetics. Most of the older antiemetics (for instance, promethazine, haloperidol, and prochlorperazine) have been tested in single studies. Their role in the control of PONV is still poorly understood. Dimenhydrinate, an antihistaminic, has been reviewed systematically (51). Its degree of efficacy seems to be similar to that of the 5-HT_3 receptor antagonists and droperidol. Transdermal scopolamine has also been reviewed systematically (55). Transdermal scopolamine applied the evening before surgery or 4 h before the end of anesthesia has an antiemetic effect. Its limitations are a 2- to 4-h onset of effect, as well as its medical contraindications and age-related considerations (56). Promethazine 12.5–25 mg IV and prochlorperazine 5–10 mg IV, administered at the end of surgery, have been shown to be effective (53,54). However, use of phenothiazines is limited in the ambulatory setting because of the resulting sedation. All three of these drugs may cause dizziness, dry mouth, and sedation. IM ephedrine is another antiemetic that has shown efficacy for inpatient and outpatient surgery (52).

Nonpharmacological Techniques. Nonpharmacologic techniques, including acupuncture, transcutaneous electrical nerve stimulation, acupoint stimulation, and acupressure, have shown antiemetic efficacy when used before surgery. The NNT for PONV prophylaxis ($\leq$6 h after surgery) is approximately 5 for these techniques (59). Hypnosis has been found to be effective when compared with placebo (60).

Lack of Evidence of Effect. Metoclopramide, when used in standard clinical doses (10 mg IV), is ineffective for PONV prophylaxis (61). Even in larger doses, metoclopramide does not appear to be an effective antiemetic (20). However, one study showed that metoclopramide 20 mg was comparable to 8 mg of ondansetron when administered at the end of laparoscopic cholecystectomy (62). Although most members of the panel agreed that metoclopramide could not be recommended as an antiemetic, agreement was not unanimous. Ginger root, a pharmacologic alternative to medical therapy, has not been found to be effective for PONV prophylaxis (63). Cannabinoids (nabilone and tetrahydrocannabinol), although promising in the control of chemotherapy-induced sickness (64), have not shown antiemetic efficacy in the PONV setting (65).

Cost-Effectiveness. The cost-effectiveness of the various antiemetics is a determinant in their use. Hill et al. (66) found that prophylactic PONV therapy in high-risk patients was more cost-effective than placebo because of the increased costs associated with nausea and vomiting. They determined that the additional costs associated with PONV in placebo patients were up to 100 times more expensive compared with prophylaxis with a generic antiemetic. The cost of treating vomiting was three times more than the cost of treating nausea. The panel estimated that each episode of emesis delays discharge from the recovery room by approximately 20 min (67). Similarly, a study evaluating dolasetron, droperidol, or no prophylaxis in high-risk patients found that prophylaxis with either of the two antiemetics was more cost-effective than no prophylaxis and subsequent rescue therapy (68). It has been suggested that PONV prophylaxis is cost-effective with the older, less expensive drugs

Table 6. Antiemetic Doses for Children

Drug	Dose	Evidence
Ondansetron	50–100 μg/kg up to 4 mg (37)	IIA
Dolasetron	350 μg/kg up to 12.5 mg (71)	V
Dexamethasone	150 μg/kg up to 8 mg (44)	IIA
Droperidol	50–75 μg/kg up to 1.25 mg (50)	IIA
Dimenhydrinate	0.5 mg/kg (51)	IIA
Perphenazine	70 μg/kg (72,73)	IA

when patients have a ≥10% risk of emesis (69). In yet another model, treatment of PONV with ondansetron was more cost-effective that prevention in both a low-risk (30%) and a high-risk (60%) setting (70). The reason for this was the frequent success rate of treating established PONV, even with small doses of ondansetron (1 mg). The panel agreed that, with equivalent efficacy and safety profiles, acquisition cost was the primary factor that differentiated the 5-HT_3 compounds from one another. The panel also recognized that many of the cost-effectiveness studies were performed in North America and may not be applicable to different health care models.

Guideline 5: Antiemetic Therapy for POV Prophylaxis in Children

The prophylactic antiemetic doses recommended for children at risk for POV are shown in Table 6. The POV rate in children can be twice as frequent as the rate in adults (5). Thus, more children than adults may be candidates for POV prophylaxis. Ondansetron has been studied extensively for POV prophylaxis in children at a dose range of 50 to 100 μg/kg. Compared with placebo, the NNT to prevent early (0–6 h) and late (0–24 h) vomiting is between 2 and 3 (37). The optimal dose for POV prophylaxis with dolasetron, as suggested by the manufacturer, is 350 μg/kg (71). Because the 5-HT_3 antagonists as a group have greater efficacy in the prevention of vomiting than nausea, they are the drugs of first choice for prophylaxis in children. When dexamethasone was used in children at a dose of 150 μg/kg, the NNT to prevent early and late vomiting was approximately 4 (44). Droperidol can also be used for the prophylaxis of POV and is administered in a dose range of 50 to 75 μg/kg. The NNT for prevention of early vomiting is approximately 5; for prevention of late vomiting, the NNT is between 4 and 5 (50). Because of the increased risk for extrapyramidal symptoms and high levels of sedation found with droperidol, the panel recommended that this drug be reserved for patients who have failed all other therapies and are being admitted to the hospital.

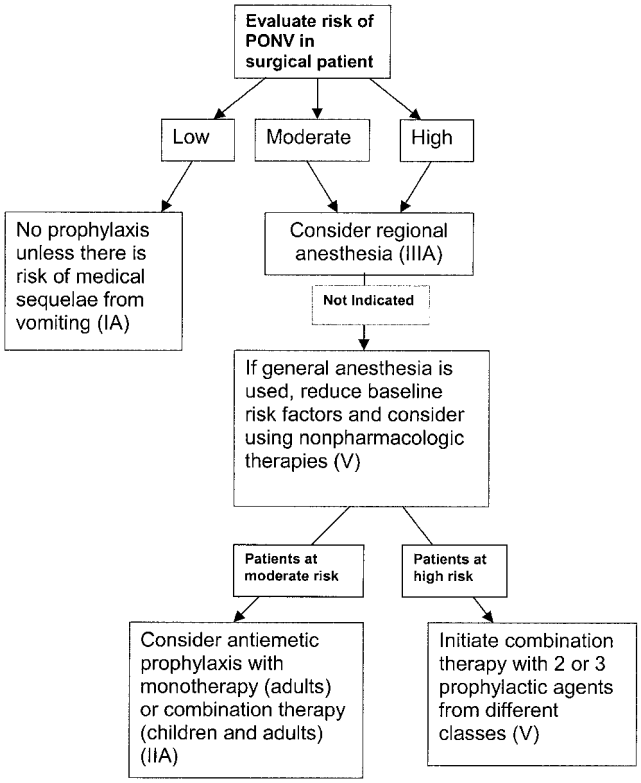

Figure 1. Algorithm for management of postoperative nausea and vomiting (PONV).

Guideline 6: Use Prophylaxis in Patients at High Risk for PONV and Consider Prophylaxis in Patients at Moderate Risk for PONV

Figure 1 illustrates a possible algorithm for PONV prophylaxis. Prophylaxis is likely to be useful only for patients at moderate to high risk for PONV. Patients at low risk for PONV are usually not given PONV prophylaxis unless they are at risk for medical sequelae from vomiting (i.e., patients with wired jaws or increased intracranial pressure or who are having fundoplication surgery).

Among patients at moderate and high risk for PONV, regional anesthesia should be considered. If general anesthesia is used, the panel recommended reduction of baseline risk factors when possible (Guideline 3). Nonpharmacologic therapies, such as acupuncture, acupressure, transcutaneous electrical nerve stimulation, or acupoint stimulation, should be considered. Antiemetics recommended for prophylaxis in adults and children are shown in Tables 5 and 6. Adults and children who are at moderate or high risk for PONV should receive combination therapy with two or three prophylactic drugs from different classes.

In general, combination therapy is superior to monotherapy for PONV prophylaxis (74,75). Drugs with different mechanisms of action should be used

Table 7. Antiemetic Treatment for Patients with Postoperative Nausea and Vomiting (PONV) Who Did Not Receive Prophylaxis or in Whom Prophylaxis Failed—Exclude Inciting Medication or Mechanical Causes of PONV (V)

Initial Therapy	Failed Prophylaxis
No prophylaxis or dexamethasone	Administer small-dose 5-HT_3 antagonist[a] (IIA)
5-HT_3 antagonist[a] plus second agent[b]	Use drug from different class (V)
Triple therapy with 5-HT_3 antagonist[a] plus two other agents[b] when PONV occurs <6 h after surgery (V)	Do not repeat initial therapy (IIIA) Use drug from different class (V) or propofol, 20 mg as needed in postanesthesia care unit (adults) (IIIB)
Triple therapy with 5-HT_3 antagonist[a] plus two other agents[b] when PONV occurs >6 h after surgery (V)	Repeat 5-HT_3 antagonist[a] and droperidol (not dexamethasone or transdermal scopolamine) Use drug from different class (V)

5-HT_3 = serotonin.
[a] Small-dose 5-HT antagonist dosing: ondansetron 1.0 mg, dolasetron 12.5 mg, granisetron 0.1 mg, and tropisetron 0.5 mg.
[b] Alternative therapies for rescue: droperiodol 0.625 mg IV, dexamethasone (2–4 mg IV), and promethazine 12.5 mg IV.

in combination to optimize efficacy. The 5-HT_3 antagonists, which have better antivomiting than antinausea efficacy, yet are associated with headache, can be used in combination with droperidol, which has greater antinausea efficacy and a protective effect against headache (9). The 5-HT_3 antagonists can also be effectively combined with dexamethasone (44). The combination of a 5-HT_3 antagonist and promethazine significantly reduces both the frequency and severity of nausea and vomiting (54). Optimal antiemetic dosing with combination therapy needs to be established. It has been suggested that, with combination therapy, dexamethasone doses should not exceed 10 mg IV (150 μg/kg in children) and droperidol doses should not exceed 1 mg IV (50 μg/kg in children) (9). When used in combination with another drug, ondansetron doses in adults typically do not exceed 4 mg and can be much smaller (50 μg/kg in both children and adults) (9).

Guideline 7: Provide Antiemetic Treatment to Patients with PONV Who Did Not Receive Prophylaxis or in Whom Prophylaxis Failed

The recommended treatment regimens for PONV are shown in Table 7. When persistent nausea and vomiting occur after the patient has left the postanesthesia care unit, the first response should be a bedside examination to exclude an inciting medication or mechanical factor. Contributing factors might include morphine patient-controlled analgesia, blood draining down the throat, or an abdominal obstruction. Once medication and mechanical factors are excluded, rescue antiemetic therapy can be initiated.

If a patient has received no prophylaxis, therapy with small-dose 5-HT_3 receptor antagonists should be initiated on the first signs of PONV (76). In general, treatment doses of the 5-HT_3 antagonists are about a quarter of those used for prophylaxis (77). Small-dose therapy includes ondansetron 1.0 mg, dolasetron 12.5 mg, granisetron 0.1 mg, and tropisetron 0.5 mg. NNTs to prevent further PONV within 24 h are between 4 and 5 (76). For all the other antiemetics, data on their therapeutic efficacy are sparse, and optimal doses are unknown. One study found that promethazine was as effective as PONV treatment in the general surgical population (78). Droperidol was not different from ondansetron as therapy for established PONV (77).

When prophylaxis with dexamethasone fails to prevent PONV, treatment with a small-dose 5-HT_3 receptor antagonist has been recommended (79). When prophylaxis with a 5-HT_3 antagonist is inadequate to prevent PONV, a 5-HT_3 antagonist should not be initiated as rescue therapy within the first 6 h after surgery because it confers no additional benefit (80). Similarly, the failure of prophylaxis with a 5-HT_3 antagonist plus dexamethasone should be treated with a drug from another class: for instance, droperidol or promethazine (78).

A triple-therapy dosing regimen (for instance, a 5-HT_3 antagonist, droperidol, and dexamethasone) has never been tested. If the patient experiences PONV symptoms despite triple prophylaxis, the triple regimen should not be repeated within the first 6 h of administration, and alternative antiemetics should be administered. Propofol, 20 mg as needed, can be considered for rescue therapy in patients still in the postanesthesia care unit (81,82). The antiemetic effect with small doses of propofol is probably brief.

When PONV occurs more than 6 h after surgery, repeat dosing of 5-HT_3 antagonists and droperidol can be considered. The optimal doses and interval for readministration of these two antiemetics remain unknown. The panel recommended that dexamethasone administration not be repeated more often than every 8 h.

Conclusion

These guidelines provide a comprehensive, evidence-based reference tool for the management of patients at risk for PONV. Not all surgical patients will benefit from antiemetic prophylaxis; thus, identification of patients who are at increased risk is imperative. The

first step in reducing PONV risk is to reduce baseline risk factors among patients at risk.

Drugs for PONV prophylaxis for adults should be considered for use as monotherapy or in combination for patients at moderate risk for PONV. There is increasing evidence that the combination of several potentially beneficial factors (multimodal approach) may lead to an improved outcome. Double and triple antiemetic combinations are recommended for patients at high risk for PONV. All prophylaxis in children at moderate or high risk for POV should be with combination therapy using a 5-HT_3 antagonist and a second drug. Antiemetic rescue therapy should be administered to patients who have an emetic episode after surgery. If PONV occurs within 6 h after surgery, patients should not receive a repeat dose of the prophylactic antiemetic. An emetic episode more than 6 h after surgery can be treated with any of the drugs used for prophylaxis except dexamethasone and transdermal scopolamine.

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