Consensus Panel Recommendations for the Management of Postoperative Nausea and Vomiting

Tong J. Gan, MB, FRCA

Postoperative nausea and vomiting (PONV) are two of the most common and unpleasant side effects following anesthesia and surgery. In the United States, more than 71 million inpatient and outpatient operative procedures are performed each year.[1] Untreated, PONV occurs in 20% to 30% of the general surgical population and in up to 70% to 80% of high-risk surgical patients.[2–4] The adverse effects of PONV range from patient-related distress to morbidity. PONV associated with ambulatory surgery increases health care costs due to unanticipated hospital admission, and accounts for 0.1% to 0.2% of these unanticipated admissions, which is significant in the United States where more than 31 million patients undergo ambulatory surgery each year.[1,5–7] It is estimated that an episode of vomiting prolongs post-anesthesia care unit (PACU) stay by about 30 min.[8] The estimated cost of PONV to a busy ambulatory surgical unit was estimated to range from $0.25 million to $1.5 million per year in lost surgical revenue.[9] The results of several studies suggest that patients not only rank the absence of PONV as being important,[10] but also rank it more important than an earlier discharge from an ambulatory surgical unit.[11] In one survey, patients were willing to pay up to US$100, at their own expense, for a completely effective antiemetic.[12]

The first PONV consensus guidelines were published in *Anesthesia & Analgesia* in 2003.[13] The current guidelines are developed under the auspices of The Society of Ambulatory Anesthesia (SAMBA).[14] The panel reviewed new literature since the previous consensus guidelines on PONV published in 2003.

GOALS OF GUIDELINES

The panel defined the following goals for the guidelines: 1) identify the primary risk factors for PONV in adults and POV in children; 2) establish factors that reduce the baseline risks for PONV; 3) determine the most effective antiemetic monotherapies and combination therapy regimens for PONV/POV prophylaxis, including pharmacologic and nonpharmacologic approaches; 4) ascertain the optimal approach to treatment of PONV with or without PONV prophylaxis; 5) determine the optimal dosing and timing of antiemetic prophylaxis; 6) evaluate the cost-effectiveness of various PONV management strategies using incremental cost-effectiveness ratio (cost of treatment A - cost of treatment B)/(success of treatment A - success of treatment B); and 7) create an algorithm to identify individuals at increased risk for PONV and to suggest effective treatment strategies.

STRENGTH OF EVIDENCE

A variety of grading systems has been proposed to document the strength of evidence of randomized and observational studies supporting a treatment. The panel decided not to grade the included literature but to base its recommendation exclusively on valid studies with a minimal risk of bias. Thus, recommendations would only be made if they were supported by randomized trials and systematic reviews of randomized trials to document efficacy and harm of antiemetic interventions, and by nonrandomized studies using logistic regression to identify risk factors of PONV.

GUIDELINE 1: IDENTIFY PATIENTS' RISK FOR PONV

Adults

Prophylaxis is indicated only in those patients undergoing surgery who are at increased risk for PONV. To determine which patients are candidates for prophylaxis, several baseline risk factors that are independent predictors of PONV have been identified. The predictors fall into 3 categories: (a) patient-specific, (b) anesthetic, and (c) surgical; these are listed in Table 1. The most prevalent patient-specific risk factors for PONV are female gender, nonsmoking status, and a history of PONV or motion sickness.[3,15–17] Other potential patient-specific risk factors include migraine, young age, anxiety, and an American Society of Anesthesiologists (ASA) low-risk classification.[18,19] Anesthetic risk factors include use of general anesthesia with volatile anesthetics, use of nitrous oxide, and postoperative use of opioids.[3,5–7,18] Patients are at increased risk for PONV during lengthy procedures performed under general anesthesia with volatile agents and with increased consumption of opioids—a response that appears to be dose-related.[2,5,7,17] The association between PONV and type of surgery is well documented; however, controversy exists over whether the association is causal. Some

Risk factors	Points
Female gender	1
Nonsmoker	1
History of PONV	1
Postoperative opioids	1
Sum	0-4

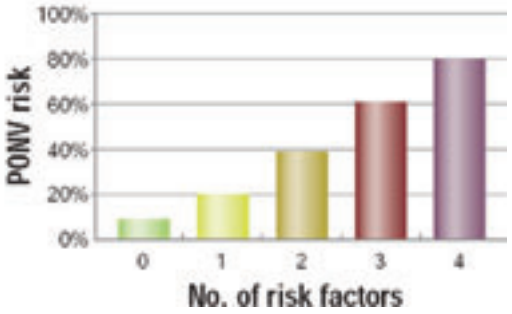


Figure 1. Simplified risk score for PONV in adults; simplified risk score data from apfel et al[3] to predict a patient's risk for PONV. When 0, 1, 2, 3, or 4 of the depicted independent predictors are present, the corresponding risk for PONV is approximately 10%, 20% 40%, 60%, or 80%, PONV, postoperative nausea and vomiting.

Risk factors	Points
Surgery ≥30 min	1
Age ≥3 years	1
Strabismus surgery	1
History of POV or PONV in relatives	1
Sum	0-4

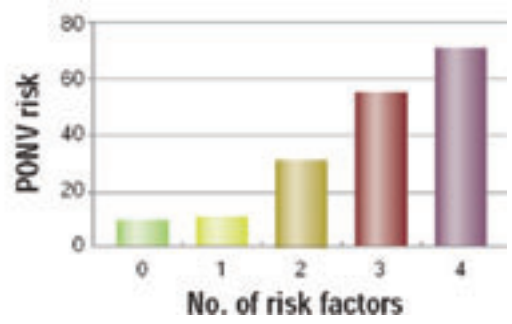


Figure 2. Simplified risk score for PONV in children; simplified risk score data from eberhart et al[20] to predict the risk for POV in children. When 0, 1, 2, 3, or 4 of the depicted independent predictors are present, the corresponding risk for PONV is approximately 9%, 10% 30%, 55%, or 70%, POV, postoperative vomiting; PONV, postoperative nausea and vomiting.

studies suggest that certain types of surgery are independent risk factors for increased PONV,[2,15,17,18,20,21] whereas others indicate that the higher incidence rates are the result of other independent risk factors that correlate with the type of surgery.[3,6,16,19,22] Risk factors that were previously thought to increase the risk for PONV but have now been shown to have no association include obesity, anxiety, and antagonizing neuromuscular block.[16,19,21–24] Because single risk factors for PONV are not sensitive or specific enough to be used to assess risk for PONV, risk models were developed to evaluate PONV risk associated with a number of independent predictors.[3,16] One of the risk models is shown in Figure 1. This simplified model from Apfel et al. shows that the greater the number of independent predictors, the higher the risk for PONV.[3] Specifically, the presence of 1 risk factor correlates with a 20% risk for PONV, and as each subsequent risk factor is added, risk increases by 20%, resulting in an 80% risk when all 4 risk factors are present. It should be noted that risk models estimate PONV risk among patient groups and cannot be used to accurately predict an individual patient's likelihood of having PONV.[19]

Children

A different set of risk factors is used to determine the potential for postoperative vomiting (POV) in children. Eberhart et al. applied a multivariable analysis to determine POV risk factors in children.[25] They identified 4 independent predictors of POV in children: (a) duration of surgery of 30 minutes or longer; (b) age of 3 years or older; (c) strabismus surgery; and (d) a positive history of POV in the patient, a parent, or a sibling. With 1 factor, the POV risk is 10%; the risk increases to 30% with 2, to 55% with 3, and to 70% when all 4 risk factors are present. This simplified risk score is shown in Figure 2. By assessing a patient's risk for PONV, clinicians can decide whether to use prophylactic antiemetics during surgery. To determine whether a patient's risk is sufficiently high to warrant the use of antiemetic prophylaxis, the expected incidence (baseline risk) is multiplied by the relative risk reduction resulting from prophylaxis. Using this calculation, clinicians can determine whether a clinically meaningful decrease in PONV risk will be achieved.[1,26] Exceptions can be made when the risk for vomiting increases medical risk (i.e., patients with wired jaws or increased intracranial pressure, those undergoing gastric or esophageal surgery) or when patients have a strong preference to avoid PONV.

GUIDELINE 2: REDUCE BASELINE RISK FACTORS FOR PONV

One way to decrease the incidence of PONV is to reduce baseline risk factors. The first step is to evaluate whether regional anesthesia can be used instead of general anesthesia. The incidence of PONV is lower in both children and adults with regional anesthesia; in some cases, the incidence is reduced ninefold.[17,27] When general anesthesia is necessary, the recommendation is to use propofol for the induction and maintenance of anesthesia. This can lower the incidence of PONV by 19%, especially within the first 6 hours (number needed to treat [NNT] = 5).[2,28] When propofol is combined with air-oxygen (total IV anesthesia [TIVA]), PONV risk is reduced approximately 25%.[2] Avoiding the use of nitrous oxide and volatile anesthetics can further reduce the incidence of PONV. Volatile anesthetics have been identified as the primary cause of PONV occurring within the first 2 hours.[5] When nitrous oxide or volatile anesthetics are

COLOR

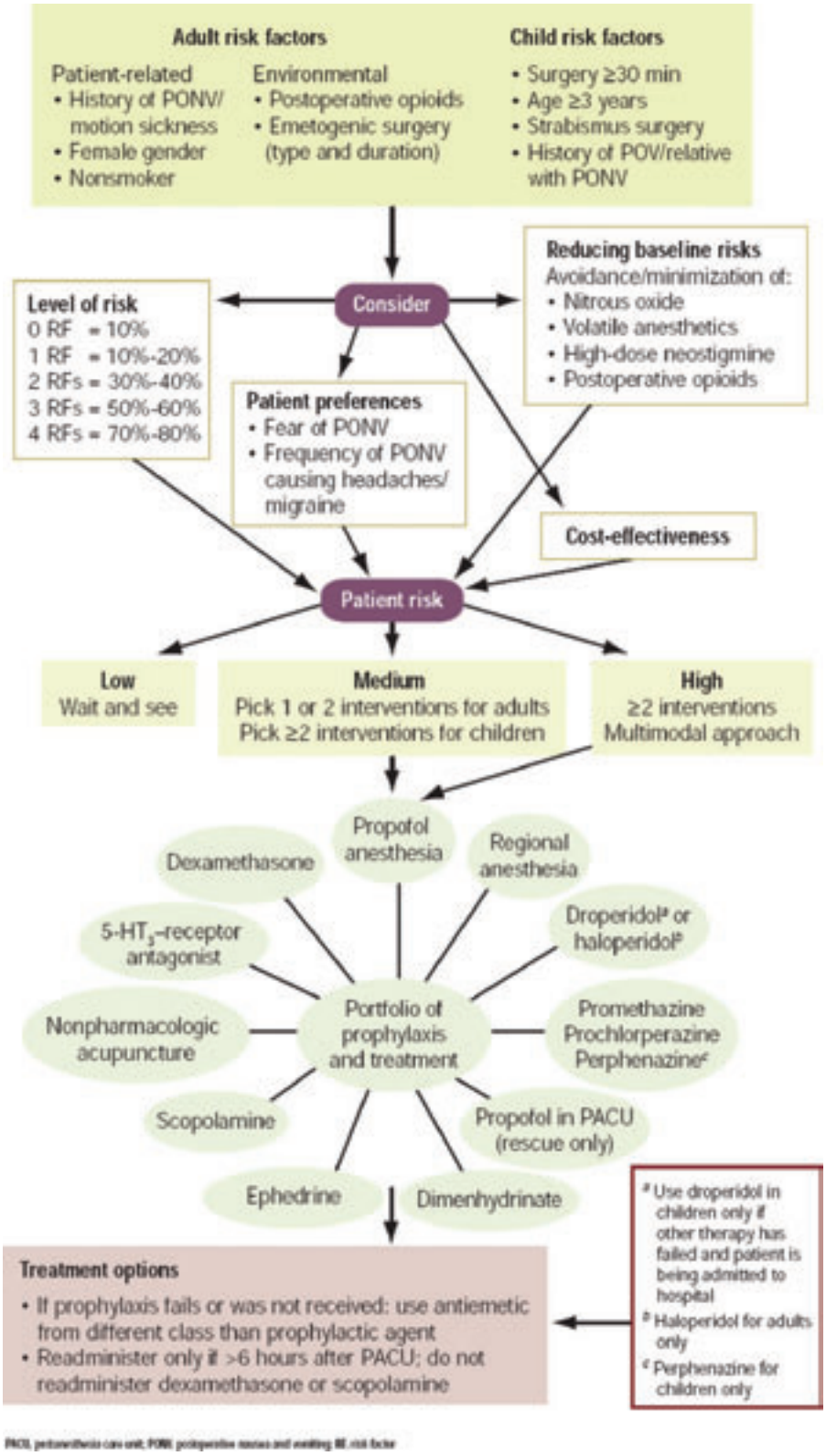
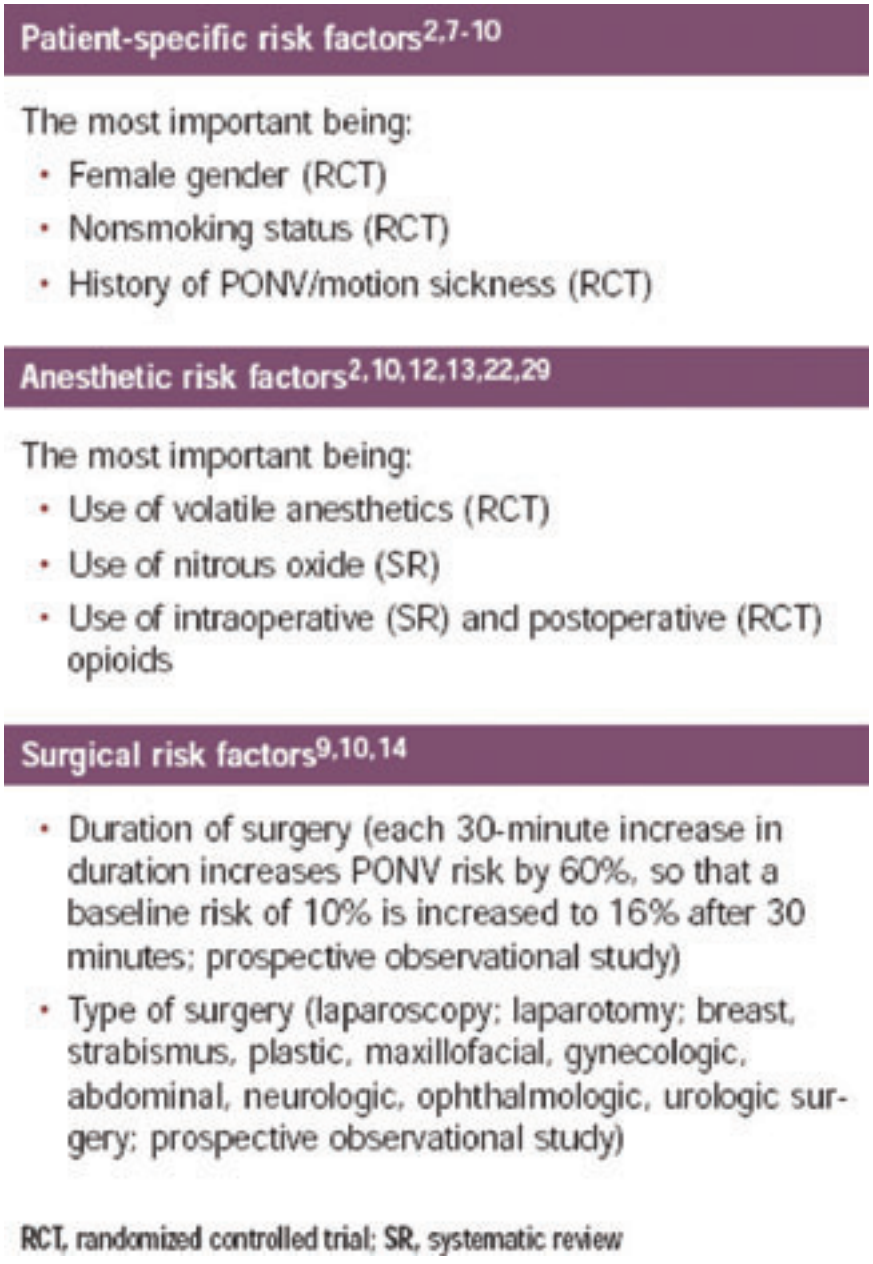


Figure 3. Algorithm for management of PONV.

administered, the incidence of PONV can be as high as 59%.[2] With avoidance of the use of nitrous oxide, PONV risk can be reduced 12%.[2,29,30] Minimizing the use of intra- and postoperative use of opioids further reduces PONV risk.[3,5,7,30] Alternatives to opioids that may have a morphine-sparing effect in the postoperative period include perioperative nonsteroidal anti-inflammatory drugs (NSAIDs) and cyclooxygenase-2 (COX-2) inhibitors.[31–33] Minimizing the use of neostigmine or lowering the dose can also reduce baseline PONV risk. High-dose neostigmine (>2.5 mg) is associated with high rates of PONV; dose reduction correlates with reduced PONV risk.[34,35] However, the administration of supplemental oxygen as a means to reduce PONV risk is not recommended because systematic reviews have demonstrated that it has little to



COLOR

Figure 4. Risk factors for PONV in adults.

F5 no effect.[36,37] Table 2 lists recommended strategies for reducing baseline risk factors.

GUIDELINE 3: ADMINISTER PONV PROPHYLAXIS BY USING 1 TO 2 INTERVENTIONS IN ADULTS AT MODERATE RISK FOR PONV

PONV prophylaxis is not recommended for all patients undergoing surgical procedures, only those considered at moderate to high risk. The PONV management algorithm in Figure 3 outlines the steps to consider when patient risk and subsequent therapy are being determined. For individuals at low risk, a wait-and-see policy is recommended. Adults at moderate risk for PONV should receive combination therapy with 1 or more prophylactic drugs from different classes. The recommended doses and timing of pharmacologic therapies for PONV are given in Table 3. It should be noted that these recommendations are evidence-based and that not all the drugs mentioned have an FDA indication for PONV.

F3 F6

5-HT3–Receptor Antagonists

Four 5-HT3–receptor antagonists have been studied in the prevention of PONV: ondansetron, dolasetron, granisetron, and tropisetron. All of these drugs are most effective when administered at the end of surgery.[38–41] Ondansetron, the most widely studied of the drugs, is recommended at an IV prophylactic dose of 4 mg. Its antivomiting effects are greater than its anti-nausea effects, with an NNT of approximately 6 in. the prevention of vomiting and an NNT of approximately 7 in. the prevention of nausea.[42] Dolasetron also has demonstrated efficacy in preventing PONV when given at an IV dose of 12.5 mg.[39] Granisetron

COLOR

- Avoidance of GA with use of regional anesthesia[9,22] (RCT)
- Use of propofol for induction and maintenance of anesthesia[3,14] (RCT/SR)
- Avoidance of nitrous oxide[2,3,24,25] (RCT/SR)
- Avoidance of volatile anesthetics[12] (RCT)
- Minimization of intraoperative (SR) and postoperative (RCT/SR) opioids[2,12,13]
- Minimization of neostigmine[29,30] (SR)
- Adequate hydration[69] (RCT)

Figure 5. Strategies to reduce baseline risk.

GA, general anesthesia; RCT, randomized controlled trial; SR, systematic review

COLOR

Drug	Dose	Evidence	Timing	Evidence
Dexamethasone	4-5 mg I.V.	SR[41-43]	At induction	RCT[43]
Dimenhydrinate	1 mg/kg I.V.	SR[50] RCT[51,52]	Unknown	N/A
Dolasetron	12.5 mg I.V.	RCT[36]	End of surgery; timing may not affect efficacy	RCT[36]
Droperidol[#]	0.625-1.25 mg I.V.	RCT[44]	End of surgery	SR[45]
Ephedrine	0.5 mg/kg IM	RCT[64]	End of surgery	RCT[64]
Granisetron	0.35-1.5 mg I.V.	RCT[34,35,86]	End of surgery	RCT[34,35]
Haloperidol	0.5-2 mg IM/I.V.	SR[49]	Unknown	N/A
Prochlorperazine	5-10 mg IM/I.V.	RCT[63]	End of surgery	RCT[63]
Promethazine	6.25-25 mg I.V.	RCT[59,96]	At induction	RCT[59,96]
Ondansetron	4 mg I.V.	RCT[81]	End of surgery	SR[33]
Scopolamine	Transdermal patch	SR[53,54]	Prior evening or 4 h before surgery	RCT[54]
Tropisetron	2 mg I.V.	RCT[40]	End of surgery	Expert opinion

Figure 6. Antiemetic doses and timing of administration to prevent PONV in adults.

Note: These recommendations are evidence-based, and not all the drugs have an FDA indication for PONV.
[#] See FDA black box warning.
N/A, not applicable; PONV, postoperative nausea and vomiting; RCT, randomized controlled trial; SR, systematic review

provides effective prophylaxis for PONV at an IV dose range of 0.35 to 1.5 mg, although a systematic review has brought some of these efficacy data into question.[43] Tropisetron is administered prophylactically at an IV dose of 2 mg.[44,45] Overall, the 5-HT3-receptor antagonists are considered equally safe.

Dexamethasone

Dexamethasone, a corticosteroid, is recommended at an IV prophylactic dose of 4 to 5 mg.[46,47] Unlike the recommended timing for the administration of most of the other prophylactic agents, which is at the end of surgery, the recommended timing for the administration of dexamethasone is at the induction of anesthesia.[48] As the large-scale IMPACT trial demonstrated, the efficacy of 4 mg of IV dexamethasone appears to be similar to that of 4 mg of IV ondansetron and 1.25 mg of IV droperidol.[2]

Butyrophenones

Until recently, droperidol was one of the preferred agents for PONV prophylaxis when given IV at a dose between 0.625 and 1.25 mg at the end of surgery.[49,50] However, a black box warning by the FDA led to a reduction in the use of this drug because of potential cardiovascular risks. It should be noted that the doses of droperidol used for the management of PONV are very low and not likely to be associated with significant cardiovascular events.[51,52] In making these recommendations, the panel registered concern about the validity of the FDA conclusion and concluded that droperidol would have been their first choice for PONV prophylaxis if not for the black box warning. Studies have shown equal efficacy rates for droperidol and ondansetron, with an NNT of approximately 5 for the prevention of nausea and vomiting within 24

COLOR

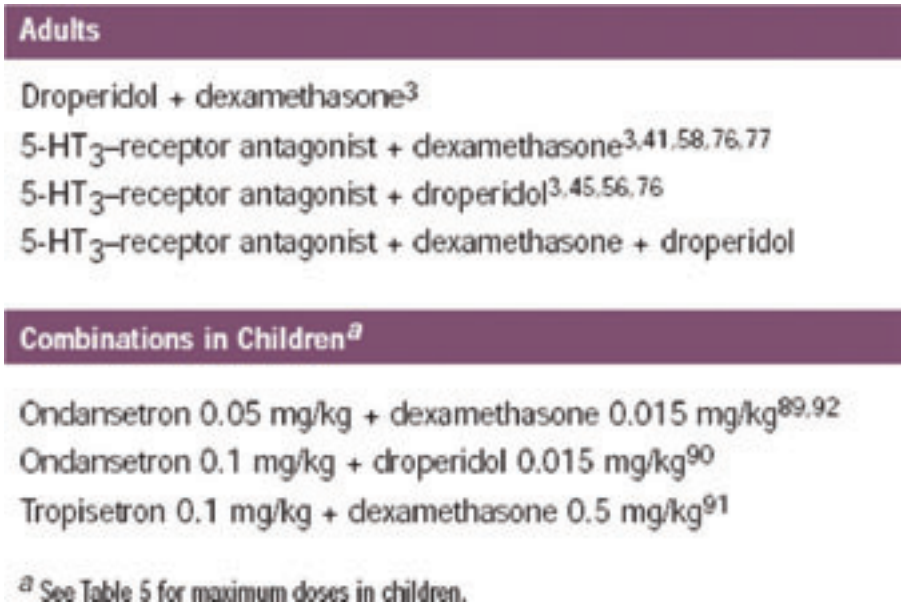


Figure 7. Pharmacologic combination therapy for adults and children.

hours.[1,3] When given with patient-controlled analgesia (PCA), the NNT of droperidol is approximately 3.48. As an alternative to droperidol, haloperidol appears to be effective at IM or IV doses much lower than those used to treat psychiatric disorders, 0.5 to 2 mg, with an NNT of between 4 and 6.49. At higher doses, haloperidol has been associated with sedation, cardiac arrhythmias, and extrapyramidal symptoms; however, in the doses used to prevent PONV, sedation did not occur, no cardiac arrhythmias were reported, and only 1 of 806 patients had extrapyramidal symptoms with a dose of 4 mg.[49] However, because haloperidol carries a risk for QTc interval prolongation, it is not recommended as first-line therapy.

Dimenhydrinate

The antihistamine dimenhydrinate, in a recommended IV dose of 1 mg/kg, has antiemetic efficacy similar to that of the 5-HT3–receptor antagonists dexamethasone and droperidol.[53–55] Data on optimal timing of administration, dose response, and side effects are lacking for dimenhydrinate.

Transdermal Scopolamine

Transdermal scopolamine, administered as a patch the evening before a scheduled surgical procedure or 4 hours before the end of anesthesia, has an NNT of 6.[56,57] Although useful as adjunctive PONV therapy, its drawback is a slow onset of effect, which can be 2 to 4 hours.

Combination Therapy

Meta-analyses have demonstrated the superior efficacy of combination therapy compared with monotherapy for PONV prophylaxis.[58,59] Whenever possible, it is preferable to optimize efficacy by combining drugs with different mechanisms of action (Table 4). For example, drugs with superior antiemetic activity, like the 5-HT3-receptor antagonists, should be used in combination with a drug like droperidol, which has greater anti-nausea efficacy and is protective against headache, a known side effect of the 5-HT3–receptor antagonists.[1] Unfortunately, there is a paucity of data on combination therapy for PONV. The 5-HT3-receptor antagonists have successfully been used in combination with dexamethasone in 1 trial and with promethazine in another; however, optimal antiemetic dosing needs to be established when the drugs are used in combination.[60,61] Evidence suggests that when combined with another drug, dexamethasone should not be given in IV doses exceeding 10 mg, droperidol should not be given in IV doses exceeding 1 mg, and ondansetron should not be given in doses exceeding 4 mg; doses of ondansetron can often be much lower.[1]

Lack of Evidence of Effect

Drugs that have been proven ineffective for PONV prophylaxis include metoclopramide (10 mg IV), ginger root, and cannabinoids (e.g., nabilone, tetrahydrocannabinol).[62–64] In addition, because of a paucity of data on promethazine at an IV dose of 12.5 to 25 mg, prochlorperazine at an IV dose of 5 to 10 mg, and ephedrine at an IV dose of 0.5 mg/kg, these drugs cannot be recommended first-line therapy.[61,65,66] Similarly, not enough data are available to support recommending hypnosis as a modality for PONV prophylaxis.

Nonpharmacologic Prophylaxis

In several clinical trials, acupuncture, acupressure, acupoint stimulation, and transcutaneous electrical nerve stimulation (TENS) had antiemetic efficacy rates comparable with that of pharmacologic therapy (NNT $\approx$ 5, <6 hours after surgery).[67–70] Stimulation of the P6 acupuncture point was as effective as the administration of ondansetron in comparisons with

F7

COLOR

Drug	Dose	Evidence
Dexamethasone	150 mcg/kg up to 5 mg	SR[41,87]
Dimenhydrinate	0.5 mg/kg up to 25 mg	SR[50]
Dolasetron	350 μmcg/kg up to 12.5 mg	RCT[83,84]
Droperidol[a]	10-15 μmcg/kg up to 1.25 mg	SR[45]
Granisetron	40 mcg/kg up to 0.6 mg	RCT[86]
Ondansetron[b]	50-100 mcg/kg up to 4 mg	SR[37,82]
Perphenazine[c]	70 mcg/kg up to 5 mg	RCT[88]
Tropisetron	0.1 mg/kg up to 2 mg	SR[39]

Note: These recommendations are evidence-based, and not all the drugs have an FDA indication for PONV.

[a] See FDA black box warning. Recommended dose is 10 to 15 mcg/kg.

[b] Approved for POV in pediatric patients aged 1 month or older.

[c] I.V. formulation of perphenazine is no longer available in the United States, only the oral formulation.

POV, postoperative vomiting; RCT, randomized controlled trial; SR, systematic review

Figure 8. Antiemetic doses for prophylaxis of PDV in children.

controls ($P = 0.006$), especially for reducing the incidence of nausea, which was 19% with P6 stimulation, 40% with ondansetron, and 79% with placebo.[68]

Novel Therapies

Several novel drugs show promise in the prevention and treatment of PONV. These include the opioid antagonists naloxone, nalmefene, and alvimopan and the neurokinin-1 (NK1) receptor antagonists CP-122721, GR205171, and aprepitant. Naloxone, when given at low doses (0.25 μg/kg per hour), decreased the incidence of PONV, reduced the need for rescue medication in adults, and reduced opioid-related side effects in children.[71,72] Nalmefene had similar effects, reducing opioid-induced nausea and vomiting and the need for rescue medication in patients receiving PCA.[73] In a placebo-controlled trial, 6 mg of alvimopan effectively reduced nausea and vomiting.[74] The NK1-receptor antagonists also proved effective in preventing PONV.CP-122721, significantly reduced vomiting both alone and in combination with ondansetron.[75] Compared with placebo, GR205171 had a significant treatment effect on vomiting ($P < 0.01$).[76] Compared with ondansetron, 40 mg of oral aprepitant showed equal efficacy in the prevention of nausea and in reducing the need for rescue medication (24 hours postoperatively) and was significantly superior in the prevention of vomiting ($P < 0.001$).[77]

GUIDELINE 4: ADMINISTER PROPHYLACTIC THERAPY WITH COMBINATION (>2) INTERVENTIONS/MULTIMODAL THERAPY IN PATIENTS AT HIGH RISK FOR PONV

Among patients at high risk for PONV, prophylaxis with combination therapy that includes 2 or more interventions is recommended (Fig. 3). In this group of patients, baseline risk factors should be reduced, regional anesthesia should be used whenever possible, and when general anesthesia is needed, factors that could increase PONV risk should be minimized or avoided. Adjunctive therapy including nonpharmacologic approaches should also be considered. The recommended antiemetics for prophylaxis in adults are shown in Table 3, and those recommended for prophylaxis in children are shown in Table 5. Combination therapies with evidence-based efficacy are shown in Table 4. F8

When combination therapy for PONV prophylaxis is being selected, drugs from different classes should be chosen to optimize their effects. Systematic reviews evaluating the efficacy of various combinations have shown that using 5-HT3–receptor antagonists in combination with either dexamethasone or droperidol is a more effective strategy than using monotherapy with any of these drugs.[2,46,58,78,79] The combination of droperidol and dexamethasone is more effective than either agent alone.[2] A comparison of the various combinations found no significant differences between a 5-HT3-receptor antagonist plus droperidol, a 5-HT3–receptor antagonist plus dexamethasone, and droperidol plus dexamethasone.[2,79] However, metoclopramide, used in combination with any of these drugs, did not reduce PONV to a greater extent than monotherapy, further evidence of the lack of support for its use.[75,80]

Scuderi et al. demonstrated the efficacy of a multimodal approach to PONV combining pharmacologic and nonpharmacologic prophylaxis as well as strategies to reduce baseline risk.[81] Prophylactic combination therapy was administered with droperidol and dexamethasone at induction and ondansetron at the end of surgery. In addition, preoperative anxiolysis, aggressive hydration, and oxygen were given. TIVA was used with propofol, remifentanil, and ketorolac. The use of nitrous oxide and neuromuscular blockade was avoided. With this approach, Scuderi et al. found

a 98% complete response rate among patients who received multimodal therapy, a 76% response rate among patients who received prophylactic antiemetic monotherapy, and a 59% response rate among those patients given a routine anesthetic plus placebo.

GUIDELINE 5: ADMINISTER PROPHYLACTIC ANTIEMETIC THERAPY TO CHILDREN AT INCREASED RISK FOR POV—AS IN ADULTS, COMBINATION THERAPY IS MOST EFFECTIVE

Children are at greater risk for POV than adults, with a rate nearly double that seen in the adult population.[82] As a consequence, POV prophylaxis should be more aggressive, consisting of combination therapy with 2 or 3 prophylactic drugs from different classes for patients at either moderate or high risk. The recommended prophylactic antiemetics for children are shown in Table 5.

The 5-HT3–receptor antagonists are the first-line therapy for the prophylaxis of POV in children because findings from meta-analyses and single studies have demonstrated their superiority to droperidol and metoclopramide. In general, the 5-HT3–receptor antagonists as a group have greater efficacy in the prevention of vomiting than of nausea, which is pivotal to preventing POV in children. Ondansetron is one of the most widely studied drugs for POV prophylaxis in children.[83,84] The only prophylactic antiemetic with a pediatric indication, ondansetron is approved for use in children aged 1 month or older.[83] The recommended dose range is 50 to 100 μg/kg.[84] Placebo-controlled trials have shown that ondansetron has an NNT between 2 and 3 to prevent early (0–6 hours) and late (0–24 hours) vomiting.[84] Dolasetron is also effective for POV prophylaxis, with an optimal dose of 350 μg/kg.[85–87] Although very few trials have been conducted in the pediatric population with the other two 5-HT3-receptor antagonists, granisetron at a dose of 40 μg/kg and tropisetron at a dose of 0.1 mg/kg appear to significantly reduce the incidence of POV in children.[45,88]

Other effective drugs for pediatric POV prophylaxis include dexamethasone at a dose of 150 μg/kg (NNT $\approx$ 4),[46,89] dimenhydrinate at a dose of 0.5 mg/kg,[55] and perphenazine at a dose of 70 μg/kg (restricted to the oral formulation because the IV formulation is no longer available in the United States).[90] Droperidol may be used in children; however, because of an increased risk for extrapyramidal symptoms and sedation, it is a last resort measure, to be used only in patients being admitted to the hospital. Although the recommended dose range is 50 to 75 μg/kg, the panel considered this too high for children and recommended instead a range of 10 to 15 μg/kg, extrapolated from adult doses (i.e., 0.625–1.25 mg).[50]

Combination therapy is more effective than monotherapy for POV prophylaxis in children.[91–94] Combinations that have demonstrated clinical efficacy are shown in Table 4. When combination therapy is administered to children, dexamethasone doses should not exceed 150 μg/kg, droperidol doses should not exceed 15 μg/kg, and ondansetron doses should not exceed 50 μg/kg.[1]

GUIDELINE 6: PROVIDE ANTIEMETIC TREATMENT TO PATIENTS WITH PONV WHO DID NOT RECEIVE PROPHYLAXIS OR IN WHOM PROPHYLAXIS FAILED

When the treatment of PONV becomes necessary, resulting from either a prior lack or failure of prophylaxis, therapy should be chosen from a pharmacologic class different from that of the initial prophylactic agent; if no prophylaxis was given, a low dose of a 5-HT3–receptor antagonist should be administered.[95,96] The 5- HT3-receptor antagonists are first-line therapy for existing PONV because they are the only drugs that have been adequately studied, and they have all been found to be equally antiemetic.[96,97] The recommended dosing for treatment with the 5-HT3-receptor antagonists is lower than that recommended for prophylaxis: 1.0 mg of ondansetron, 0.1 mg of granisetron, and 0.5 mg of tropisetron (NNT = 4–5).[84,96] Lower doses of dolasetron have not been studied, so 12.5 mg is recommended for treatment. Other therapies for established nausea and vomiting include 2 to 4 mg of IV dexamethasone, 0.625 mg of IV droperidol, and 6.25 to 12.5 mg of IV promethazine.[95,97,98] Propofol, administered in doses of 20 mg as needed, can be considered for rescue therapy in patients still in the PACU and has been found as effective as ondansetron.[99,100] Among patients who have opioid-induced nausea or vomiting, the addition of 2.5 mg of droperidol to every 100 mg of morphine in a PCA device appears to reduce PONV.[101]

If prophylaxis has been given and has failed, the same medication should not be repeated within the first 6 hours after the patient has left the PACU, because this will confer no additional benefit.[102] If more than 6 hours has elapsed, a repeat dose of a 5-HT3-receptor antagonist—droperidol or haloperidol—may be attempted, but only if triple therapy has been used for prophylaxis and no alternatives are available for rescue medication (Fig. 3). The readministration of dexamethasone or transdermal scopolamine is not recommended within 24 hours.

Post-discharge Nausea and Vomiting

Post-discharge nausea and vomiting (PDNV) is a substantial problem following ambulatory surgery, affecting approximately one third of patients.[103] Prophylactic antiemetic therapy may be given before discharge in patients at high risk for PDNV; however, antiemetics with a short half-life may prove ineffective. Prophylactic combination therapy appears to be the best approach, with an NNT of approximately 5 versus an NNT of approximately 12 to 13 for monotherapy with 4 mg of ondansetron or 4 to 10 mg of dexamethasone.[103]

Other effective strategies for reducing the incidence of PDNV include substituting propofol for inhalational anesthesia ($P < 0.05$), using orally disintegrating ondansetron tablets, acupoint stimulation of P6, and transdermal scopolamine.[56,104–106] Droperidol appears to be ineffective at preventing PDNV at a dose of <1 mg, and inadequate information is available to evaluate droperidol at a dose of 1 mg or higher.[103]

SUMMARY

Identification of patients at increased risk for PONV allows targeting antiemetic prophylaxis to those who will benefit most from it. No prophylaxis is warranted for patients at low risk for PONV unless there is risk of medical sequelae from vomiting. The first step in reducing PONV risk is to reduce baseline risk factors. For patients at moderate risk, antiemetics should be used in combination for PONV prophylaxis. The adoption of a multimodal approach to the management of PONV should be considered in patients at high risk for PONV. In patients who develop PONV despite receiving prophylaxis, an antiemetic acting at a different receptor should be used for rescue within the first 6 hours following surgery. After 6 hours, PONV can be treated with any of the drugs used for prophylaxis except dexamethasone and scopolamine.

ACKNOWLEDGMENT

The author wishes to thank SAMBA PONV Consensus Panel members for their significant contributions to the guidelines.

REFERENCES

1. Tramer MR. A rational approach to the control of postoperative nausea and vomiting: evidence from systematic reviews. Part I. Efficacy and harm of antiemetic interventions, and methodological issues. Acta Anaesthesiol Scand 2001;45:4–13
2. Apfel CC, Korttila K, Abdalla M. A factorial trial of six interventions for the prevention of postoperative nausea and vomiting [see comment]. N Engl J Med 2004;350:2441–51
3. Apfel CC, Laara E, Koivuranta M. A simplified risk score for predicting postoperative nausea and vomiting: conclusions from cross-validations between two centers. Anesthesiology 1999;91:693–700
4. Tramer MR. Strategies for postoperative nausea and vomiting. Best Pract Res Clin Anaesthesiol 2004;18:693–701
5. Apfel CC, Kranke P, Katz MH. Volatile anaesthetics may be the main cause of early but not delayed postoperative vomiting: a randomized controlled trial of factorial design. Br J Anaesth 2002;88:659–68
6. Choi DH, Ko JS, Ahn HJ. A Korean predictive model for postoperative nausea and vomiting. J Korean Med Sci 2005;20:811–5
7. Roberts GW, Bekker TB, Carlsen HH. Postoperative nausea and vomiting are strongly influenced by postoperative opioid use in a dose-related manner. Anesth Analg 2005; 101:1343–8
8. Habib AS, Chen Y, Taguchi A. Postoperative nausea and vomiting following inpatient surgeries in a teaching hospital: a retrospective database analysis. Curr Med Res Opin 2006;22:1093–9
9. Hill RP, Lubarsky DA, Phillips-Bute B. Cost-effectiveness of prophylactic antiemetic therapy with ondansetron, droperidol, or placebo. Anesthesiology 2000;92:958–67
10. Gold B, Kitz DS, Lecky JH. Unanticipated admission to the hospital following ambulatory surgery. JAMA 1989;262:3008–10
11. Philip BK. Patients' assessment of ambulatory anesthesia and surgery. J Clin Anesth 1992;4:355–8
12. Gan T, Sloan F, Dear G. How much are patients willing to pay to avoid postoperative nausea and vomiting? Anesth Analg 2001;92:393–400
13. Gan TJ, Meyer T, Apfel CC. Consensus guidelines for managing postoperative nausea and vomiting. Anesth Analg 2003;97:62–71
14. Gan T, Meyer T, Apefel CC. Society for Ambulatory Anesthesia guidelines for the management of postoperative nausea and vomiting. Anesth Analg 2007;105:1615–28
15. Cohen MM, Duncan PG, DeBoer DP, Tweed WA. The postoperative interview: assessing risk factors for nausea and vomiting. Anesth Analg 1994;78:7–16
16. Koivuranta M, Laara E, Snare L, Alahuhta S. A survey of postoperative nausea and vomiting. Anaesthesia 1997;52:443–9
17. Sinclair DR, Chung F, Mezei G. Can postoperative nausea and vomiting be predicted? Anesthesiology 1999;91:109–18
18. Stadler M, Bardaiu F, Seldel L, Boogaerts JG. Difference in risk factors for postoperative nausea and vomiting. Anesthesiology 2003;98:46–52
19. Van den Bosch JE, Moons KG, Bonsel GJ, Kalkman CJ. Does measurement of preoperative anxiety had added value for predicting postoperative nausea and vomiting. Anesth Analg 2005;100:1525–32
20. Apfel CC, Greim CA, Haubitz I. The discriminating power of a risk score for postoperative vomiting in adults undergoing various types of surgery. Acta Anaesthesiol Scand 1998;42:502–9
21. Apfel CC, Kranke P, Eberhart LH. Comparison of surgical site and patient's history with a simplified risk score for the prediction of postoperative nausea and vomiting. Anaesthesia 2004;59:1078–82
22. Apfel CC, Greim CA, Haubitz I. A risk score to predict the probability of postoperative vomiting in adults. Acta Anaesthesiol Scand 1996;42:495–501
23. Cheng CR, Sessler DI, Apfel CC. Does noestigmine administration produce a clinically important increase in postoperative nausea and vomiting? Anesth Analg 2005;101:1349–55
24. Kranke P, Apefel CC, Papenfuss T. An increased body mass index is no risk factor for postoperative nausea and vomiting: a systematic review and results of original data. Acta Anaesthesiol Scand 2001;45:160–6
25. Eberhart LH, Geldner G, Kranke P. The development and validation of a risk score to predict the probability of postoperative vomiting in pediatric patients. Anesth Analg 2004; 99:1630–7
26. Tramer M, Walder B. Number needed to treat (or harm). World J Surg 2005;29:576–81
27. Khalil SN, Farag A, Hanna E. Regional analgesia combined with avoidance of narcotics may reduce the incidence of postoperative vomiting in children. Middle East J Anesthesiol 2005;18:123–32
28. Visser K, Hassink EA, Bonsel GJ. Randomized controlled trial of total intravenous anesthesia with propofol versus inhalation anesthesia with isoflurane-nitrous oxide: postoperative nausea and vomiting and economic analysis. Anesthesiology 2001;95:616–26
29. Tramer M, Moore A, McQuay H. Omitting nitrous oxide in general anaesthesia: meta-analysis of intraoperative awareness and postoperative emesis in randomized controlled trials. Br J Anaesth 1996;76:186–93
30. Tramer M, Moore A, McQuay H. Meta-analytic comparison of prophylactic antiemetic efficacy for postoperative nausea and vomiting: propofol anaesthesia vs omitting nitrous oxide vs total i.v. anaesthesia with propofol. Br J Anaesth 1997;78:256–9
31. Elia N, Lysakowski C, Tramer M. Does multimodal analgesia with acetaminophen, nonsteroidal antiinflammatory drugs, or selective cyclooxygenase-2 inhibitors and patient-controlled analgesia morphine offer advantages over morphine alone? Meta-analyses of randomized trials. Anesthesiology 2005;103: 1296–304
32. Gan TJ, Joshi GP, Zhao SZ. Presurgical intravenous paracoxib sodium and follow-up oral valdecoxib for pain management after laparoscopic cholecystectomy surgery reduces opioid requirements and opioid related adverse effects. Acta Anaesthesiol Scand 2004;48:1194–207
33. Marret E, Kurdi O, Zufferey P, Bonnet F. Effects of nonsteroidal antiinflammatory drugs on patient-controlled analgesia morphine side efffects: meta-analysis of randomized controlled trials. Anesthesiology 2005;102:1249–60
34. Ho KM, Ismail H, Lee KC, Branch R. Use on intrathecal neostigmine as an adjunct to other spinal medications in perioperative and peripartum analgesia: a meta-analysis. Anaesth Intensive Care 2005;33:41–53

35. Tramer MR, Fuchs-Buder T. Omitting antagonism of neuromuscular block: effect on postoperative nausea and vomiting and risk of residual paralysis. A systematic review. Br J Anaesth 1999;82:379–86
36. Kranke P, Morin A, Apefel CC. A qualititative systematic review on supplemental perioperative oxygen to reduce the incidence of postoperative nausea and vomiting. Eur J Anaesthesiol 2005;22(suppl 34):1–222
37. Orhan-Sungur M, Sessler DI, Kranke P, Apfel CC. Supplemental oxygen does not reduce postoperative nausea and vomiting: a systematic review of randomized controlled trials. Anesthesiology 2005;103:A626
38. D'Angelo R, Philip B, Gan TJ. A randomized, double-blind, close-ranging, pilot study of intravenous granisetron in the prevention of postoperative and vomiting in patients abdominal hysterectomy. Eur J Anaesthesiol 2005;774–9
39. Graczyk SG, McKenzie R, Kallar S. Intravenous dolasetron for the prevention of postoperative nausea and vomiting after outpatient laparoscopic gynecologic surgery. Anesth Analg 1997;84:325–30
40. Mikawa K, Takao Y, Nishina K. Optimal dose of granisetron for prophylaxis against postoperative emesis after gynecological surgery. Anesth Analg 1997;85:652–6
41. Sun R, Klein KW, White PF. The effect of timing of ondansetron administration in outpatients undergoing otolaryngologic surgery. Anesth Analg 1997;84:331–6
42. Tramer MR, Reynolds DJ, Moore RA, McQuay HJ. Efficacy, dose-response, and safety of ondansetron in prevention of postoperative nausea and vomiting: a quantitative systematic review of randomized placebo-controlled trials. Anesthesiology 1997;87:1277–89
43. Kranke P, Apfel CC, Eberhart LH. The influence of a dominating centre on a quantitative systematic review of granisetron for preventing postoperative nausea and vomiting. Acta Anaesthesiol Scand 2001;45:659–70
44. DiBruijn KM. Tropisetron. Drugs 1992;43(suppl 3):11–22
45. Kranke P, Eberhart LH, Apefel CC. Tropisetron for prevention of postoperative nausea and vomiting: a quantitative systematic review. Anaesthesist 2002;51:805–14
46. Henzi I, Walder B, Tramer MR. Dexamethasone for the prevention of postoperative nausea and vomiting: a quantitative systematic review. Anesth Analg 2000;90:186–94
47. Wang JJ, Ho ST, Lee SC. The use of dexamethasone for preventing postoperative nausea and vomiting in females undergoing thyroidectomy: a dose-ranging study. Anesth Analg 2000;91:1404–7
48. Wang JJ, Ho ST, Tzeng JI, Tang CS. The effect of timing of dexamethasone administration on its efficacy as a prophylactic antiemetic for postoperative nausea and vomiting. Anesth Analg 2000;91:136–9
49. Fortney JT, Gan TJ, Graczyk S. A comparison of the efficacy, safety, and patient satisfaction of ondansetron versus droperidol as antiemetics for elective outpatient surgical procedures. S3A-409 and S3A-410 Study Groups. Anesth Analg 1998;86:731–8
50. Henzi I, Sonderegger J, Tramer MR. Efficacy, dose-response, and adverse effects of droperidol for prevention of postoperative nausea and vomiting. Can J Anaesth 2000;47:537–51
51. Charbit B, Albaladejo P, Funck-Brentano C. Prolongation of QTc interval after postoperative nausea and vomiting treatment by droperidol or ondansetron. Anesthesiology 2005;102:1081–2
52. White PF, Song D, Abrao J. Effect of low-dose droperidol on the QT interval during and after general anesthesia: a placebo-controlled study. Anesthesiology 2005;102:1101–5
53. Eberhart LH, Seeling W, Hartschuh T. Droperidol and dimenhydrinate alone or in combination for the prevention of post-operative nausea and vomiting after nasal surgery in male patients. Eur J Anaesthesiol 1999;16:790–5
54. Kothari SN, Boyd WC, Bottcher ML, Lambert PJ. Antiemetic efficacy of prophylactic dimenhydrinate (Dramamine) vs ondansetron (Zofran): a randomized, prospective trial inpatients undergoing laparoscopic cholecystectomy. Surg Endosc 2000;14: 926–9
55. Kranke P, Morin AM, Roewer N, Eberhart LHJ. Dimenhydrinate for prophylaxis of postoperative nausea and vomiting: a meta-analysis of randomized controlled trials. Acta Anaesthesiol Scand 2002;46:238–44
56. Bailey PL, Streisand JB, Pace NL. Transdermal scopolamine reduces nausea and vomiting after outpatient laparoscopy. Anesthesiology 1990;72:977–80
57. Kranke P, Morin AM, Roewer N. The efficacy and safety of transdermal scopolamine for the prevention of postoperative nausea and vomiting: a quantitative systematic review. Anesth Analg 2002;95:133–43
58. Eberhart LH, Morin AM, Bothner U, Georgieff M. Droperidol and 5-HT3-receptor antagonists, alone or in combination, for prophylaxis of postoperative nausea and vomiting: a meta-analysis of randomised controlled trials. Acta Anaesthesiol Scand 2000;44:1252–7
59. Habib AS, Gan TJ. Combination therapy for postoperative nausea and vomiting: a more effective prophylaxis? Ambul Surg 2001;9:59–71
60. Gan TJ, Coop A, Philip B. A randomized, double-blind study of granisetron plus dexamethasone vs ondansetron plus dexamethasone to prevent postoperative nausea and vomiting in patients undergoing abdominal hysterectomy. Anesth Analg 2005;101:1323–9
61. Khalil S, Philbrook L, Rabb M. Ondansetron/promethazine combination or promethazine alone reduces nausea and vomiting after middle ear surgery. J Clin Anesth 1999;11:596–600
62. Ernst E, Pittler MH. Efficacy of ginger for nausea and vomiting: a systematic review of randomized clinical trials. Br J Anaesth 2000;84:367–71
63. Henzi I, Walder B, Tramer MR. Metoclopramide in the prevention of postoperative nausea and vomiting: a quantitative systematic review of randomized, placebo-controlled studies. Br J Anaesth 1999;83:761–71
64. Tramer MR, Carroll D, Campbell FA. Cannabinoids for control of chemotherapy induced nausea and vomiting: quantitative systematic review. BMJ 2001;323:16–21
65. Chen JJ, Frame DG, White TJ. Efficacy of ondansetron and prochlorperazine for the prevention of postoperative nausea and vomiting after total hip replacement or total knee replacement procedures: a randomized, double-blind, comparative trial [published erratum appears in Arch Intern Med 1999 Mar 22;159(6):615]. Arch Intern Med 1998;158:2124–8
66. Rothenberg DM, Parnass SM, Litwack K. Efficacy of ephedrine in the prevention of postoperative nausea and vomiting. Anesth Analg 1991;72:58–61
67. Boehler M, Mitterschiffthaler G, Schlager A. Korean hand acupressure reduces postoperative nausea and vomiting after gynecological laparoscopic surgery. Anesth Analg 2002;94: 872–5
68. Gan TJ, Jiao KR, Zenn M, Georgiade G. A randomized controlled comparison of electro-acupoint stimulation or ondansetron versus placebo for the prevention of postoperative nausea and vomiting. Anesth Analg 2004;99:1070–5
69. Lee A, Done ML. The use of nonpharmacologic techniques to prevent postoperative nausea and vomiting: a meta-analysis. Anesth Analg 1999;88:1362–9
70. Lee A, Done ML. Stimulation of the wrist acupuncture point P6 for preventing postoperative nausea and vomiting. Cochrane Database Syst Rev 2004;3:CD003281
71. Gan TJ, Ginsberg B, Glass PS. Opioid-sparing effects of a low-dose infusion of naloxone in patient-administered morphine sulfate. Anesthesiology 1997;87:1075–81
72. Maxwell LG, Kaufmann SC, Bitzer S. The effects of a small dose naloxone infusion on opioid induced side effects and analgesia in children and adolescents treated with intravenous patient controlled analgesia: a double blind, prospective, randomized, controlled study. Anesth Analg 2005;100:953–8
73. Joshi GP, Duffy L, Chehade J. Effects of prophylactic nalmefene on the incidence of morphine-related side effects in patients receiving intravenous patient-controlled analgesia. Anesthesiology 1999;90:1007–11
74. Taguchi A, Sharma N, Saleem RM. Selective postoperative inhibition of gastrointestinal opioid receptors. N Engl J Med 2001;345:935–40
75. Gesztesi Z, Scuderi PE, White PF. Substance P (Neurokinin-1) antagonist prevents postoperative vomiting after abdominal hysterectomy procedures. Anesthesiology 2000; 93:931–7
76. Diemunsch P, Schoeffler P, Bryssine B. Antiemetic activity of the NK1 receptor antagonist GR205171 in the treatment of established postoperative nausea and vomiting after major gynaecological surgery. Br J Anaesth 1999;82:274–6

77. Gan TJ, Apfel CC, Kovac A. A randomized, double blind comparison of the NK1 antagonist aprepitant vs ondansetron for the prevention of postoperative nausea and vomiting. Anesth Analg 2007:1082–9
78. Eberhart LH, Morin AM, Georgieff M. Dexamethasone for prophylaxis of postoperative nausea and vomiting: a meta-analysis of randomized controlled studies. Anaesthesist 2000;49:713–20
79. Habib AS, El-Moalem HE, Gan TJ. The efficacy of the 5-HT3 receptor antagonists combined with droperidol for PONV prophylaxis is similar to their combination with dexamethasone: a meta-analysis of randomized controlled trials. Can J Anaesth 2004;51:311–9
80. Eberhart LH, Seeling W, Ulrich B. Dimenhydrinate and metoclopramide alone or in combination for prophylaxis of PONV. Can J Anaesth 2000;47:780–5
81. Scuderi PE, James RL, Harris L, Mims GR 3rd. Multimodal antiemetic management prevents early postoperative vomiting after outpatient laparoscopy. Anesth Analg 2000;91:1408–14
82. Lerman J. Surgical and patient factors involved in postoperative nausea and vomiting [Review]. Br J Anaesth 1992;69:24S–32S
83. Khalil SN, Roth AG, Cohen IT. A double blind comparison of intravenous ondansetron and placebo for preventing postoperative emesis in 1 to 24 month old pediatric patients after surgery under general anesthesia. Anesth Analg 2005;101: 356–61
84. Tramer MR, Moore RA, Reynolds DJ, McQuay HJ. A quantitative systematic review of ondansetron in treatment of established postoperative nausea and vomiting. BMJ 1997; 314:1088–92
85. Olutoye O, Jantzen EC, Alexis R. A comparison of the costs and efficacy of ondansetron and dolasetron in the prophylaxis of postoperative vomiting in pediatric patients undergoing ambulatory surgery. Anesth Analg 2003;97:390–6
86. Sukhani R, Pappas AL, Lurie J. Ondansetron and dolasetron provide equivalent postoperative vomiting control after ambulatory tonsillectomy in dexamethasone-pretreated children. Anesth Analg 2002;95:1230–5
87. Wagner D, Pandit U, Voepel-Lewis T, Weber M. Dolasetron for the prevention of postoperative vomiting in children undergoing strabismus surgery. Paediatr Anaesth 2003;13:522–6
88. Cieslak GD, Watcha MF, Phillips MB, Pennant JH. The dose-response relation and cost-effectiveness of granisetron for the prophylaxis of pediatric postoperative emesis. Anesthesiology 1996;85:1076–85
89. Madan R, Bhatia A, Chakithandy S. Prophylactic dexamethasone for postoperative nausea and vomiting in pediatric strabismus surgery: a dose ranging and safety evaluation study. Anesth Analg 2005;100:1622–6
90. Splinter WM, Rhine EJ. Prophylaxis for vomiting by children after tonsillectomy: ondansetron compared with perphenazine [comment]. Br J Anaesth 1998;80:155–8
91. Holt R, Rask P, Coulthard KP. Tropisetron plus dexamethasone is more effective than tropisetron alone for the prevention of postoperative nausea and vomiting in children undergoing tonsillectomy. Paediatr Anaesth 2000;10:181–8
92. Shende D, Bharti N, Kathirvel S, Madan R. Combination of droperidol and ondansetron reduces PONV after pediatric strabismus surgery more than single drug therapy. Acta Anaesthesiol Scand 2001;45:756–60
93. Splinter WM. Prevention of vomiting after strabismus surgery in children: dexamethasone alone vs dexamethasone plus low-dose ondansetron. Paediatr Anaesth 2001;11:591–5
94. Splinter WM, Rhine EJ. Low-dose ondansetron with dexamethasone more effectively decreases vomiting after strabismus sugery in children than does high-dose ondansetron. Anesthesiology 1998;88:72–5
95. Habib AS, Gan TJ. The effectiveness of rescue antiemetics after failure of prophylaxis with ondansetron or droperidol: a preliminary report. J Clin Anesth 2005;17:62–5
96. Kazemi-Kjelberg F, Henzi I, Tramer M. Treatment of established postoperative nausea and vomiting: a quantitative systemic review. BMC Anesthesiol 2001;1:2
97. Meyer TA, Robertson C, Raab MH. Dolasetron vs ondansetron for the treatment of postoperative nausea and vomiting. Anesth Analg 2005;100:373–7
98. Habib AS, Breen TW, Chukwurah CN, Gan TJ. Dose response of promethazine for the treatment of postoperative nausea and vomiting. Anesthesiology 2004;101:A47
99. Gan TJ, El-Molem H, Ray J, Glass PS. Patient-controlled antiemesis: a randomized, double-blind comparison of two doses of propofol versus placebo. Anesthesiology 1999;90:1564–70
100. Unlugenc H, Guler T, Gunes Y, Isik G. Comparative study of the antiemetic efficacy f ondansetron, propofol and midazolam in the early postoperative period. Eur J Anaesthesiol 2004; 21:60–5
101. Culebras X, Corpataux JB, Gaggero G, Tramer MR. The antiemetic efficacy of droperidol added to morphine patient-controlled analgesia: a randomized, controlled, multicenter dose-finding study. Anesth Analg 2003;97:816–21
102. Kovac AL, O'Connor TA, Pearman MH. Efficacy of repeat intravenous dosing of ondansetron in controlling postoperative nausea and vomiting: a randomized, double-blind, placebo-controlled multicenter trial. J Clin Anesth 1999; 11:453–9
103. Gupta A, Wu CL, Elkassabany N. Does the routine prophylactic use of antiemetics affect the incidence of postdischarge nausea and vomiting following ambulatory surgery? A systematic review of randomized controlled trials. Anesthesiology 2003;99:488–95
104. Gan TJ, Franiak R, Reeves J. Ondansetron orally disintegrating tablet versus placebo for the prevention of postdischarge nausea and vomiting after ambulatory surgery. Anesth Analg 2002;94:1199–1200
105. Gupta A, Stierer T, Zuckerman R. Comparison of recovery profile after ambulatory anesthesia with propofol, isoflurane, sevoflurane and desflurane: a systematic review. Anesth Analg 2004;98:632–41
106. Zarate E, Mingus M, White PF. The use of transcutaneous acupoint electrical stimulation for preventing nausea and vomiting after laparoscopic surgery. Anesth Analg 2001;92:629–35

AUTHOR QUERIES

AUTHOR PLEASE ANSWER ALL QUERIES **1**