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Guideline for the Management of Postoperative Nausea and Vomiting

This guideline has been approved by Executive and Council of the Society of Obstetricians and Gynaecologists of Canada.

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Abstract

Objective: To provide recommendations for the management of postoperative nausea and vomiting (PONV), which may affect as many as 30% of patients.

Methods and Evidence: Medline, PubMed, and the Cochrane Database were searched for articles published in English from 1995 to 2007. Recognizing that we must work as a team to optimize the care of our patients perioperatively, this guideline was written in partnership with anaesthesiologists.

Options: The areas of clinical practice considered in formulating this guideline are prevention and prophylaxis, treatment, both medical and alternative, and patient education.

Outcomes: Implementation of this guideline should optimize the prevention of and prophylaxis against PONV and the prompt treatment of women who suffer from PONV following gynaecologic surgery. Increased awareness of options for management should help minimize the effects of PONV.

Benefits, Harms, and Costs: PONV results not only in increased patient discomfort and dissatisfaction but also in increased costs related to length of hospital stay. Cost of medications to prevent and treat PONV must be weighed against improved surgical experience for the patient and decreased costs to the system.

Values: Recommendations were made according to the guidelines developed by the Canadian Task Force on Preventive Health Care.

Recommendations

1. Physicians should be aware of the risk factors associated with PONV, and the baseline risks should be reduced whenever possible. (III-A)
2. When the choice is available, patients should be advised that the risk of PONV decreases when regional rather than general anaesthesia is administered. (III-A)
3. The perioperative use of opioids should be minimized. Surgeons should evaluate the risks/benefits of opioid administration in light of the increased risk of PONV. (III-B)
4. Prophylactic antiemetics should be administered to patients with moderate or high risk of developing PONV. (II-1A)
5. In patients with a high risk of developing PONV, combination antiemetic therapy should be considered. (III-B)
6. Acupoint electrical stimulation may be used as an alternative or adjuvant therapy for prevention of PONV. (II-1A)
7. For patients with PONV who did not receive prophylaxis or in whom prophylaxis failed, antiemetic treatment should be administered as soon as feasible. (III-A)
8. When prophylaxis with one drug has failed, a repeat dose of this drug should not be initiated as a rescue therapy; instead, a drug from a different class of antiemetic drugs should be administered. (III-A)
9. As patients who undergo surgery in surgical daycare units may have PONV after they are discharged, they should be given instructions for its management. (III-B)
10. Patients at high risk of developing PDNV should be provided with rescue treatment. (III-B)

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INTRODUCTION

Postoperative nausea and vomiting, defined as nausea and/or vomiting occurring within 24 hours after surgery, affects between 20% and 30% of patients.[1–4] As many as 70% to 80% of patients at high risk may be affected.[5] The etiology of PONV is thought to be multifactorial, involving individual, anaesthetic, and surgical risk factors.[2,5,6] PONV results in increased patient discomfort and dissatisfaction[6] and in increased costs related to length of hospital stay. One study revealed that the time to discharge was increased by 25% in patients with PONV.[7] Serious medical complications such as pulmonary aspiration, although uncommon, are also associated with vomiting.[6]

Table 1. Key to evidence statements and grading of recommendations, using the ranking of the Canadian Task Force on Preventive Health Care

Quality of Evidence Assessment*	Classification of Recommendations†
I: Evidence obtained from at least one properly randomized controlled trial	A. There is good evidence to recommend the clinical preventive action
II-1: Evidence from well-designed controlled trials without randomization	B. There is fair evidence to recommend the clinical preventive action
II-2: Evidence from well-designed cohort (prospective or retrospective) or case-control studies, preferably from more than one centre or research group	C. The existing evidence is conflicting and does not allow to make a recommendation for or against use of the clinical preventive action; however, other factors may influence decision-making
II-3: Evidence obtained from comparisons between times or places with or without the intervention. Dramatic results in uncontrolled experiments (such as the results of treatment with penicillin in the 1940s) could also be included in this category	D. There is fair evidence to recommend against the clinical preventive action
III: Opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees	E. There is good evidence to recommend against the clinical preventive action
	L. There is insufficient evidence (in quantity or quality) to make a recommendation; however, other factors may influence decision-making

*The quality of evidence reported in these guidelines has been adapted from The Evaluation of Evidence criteria described in the Canadian Task Force on Preventive Health Care.[75]
†Recommendations included in these guidelines have been adapted from the Classification of Recommendations criteria described in the The Canadian Task Force on Preventive Health Care.[75]

PONV is a significant problem for patients: in one study, patients were more concerned about PONV than about postoperative pain[8]; in another, patients were willing to spend up to US $100 for an effective antiemetic treatment.[9]

Several thousand studies examining PONV have been published, and several hundred new papers are published each year on the topic. Guidelines for the prevention and management of PONV have been published by anaesthetic journals and societies.[10–12]

Management of PONV for gynaecological patients in most hospitals continues to be on an ad hoc basis. The aim of these guidelines is to provide information on the management of PONV in gynaecological patients.

PHYSIOLOGY OF NAUSEA AND VOMITING

Primary control of nausea and vomiting arises from the vomiting centre, located in the medulla. The five primary afferent pathways involved in stimulating the vomiting centre are:

1. the chemoreceptor triggering zone,
2. the vagal mucosal pathway in the gastrointestinal system,
3. neuronal pathways from the vestibular system,
4. reflex afferent pathways from the cerebral cortex C2,3, and
5. midbrain afferents.

Stimulation of one of these afferent pathways can activate the vomiting centre via cholinergic (muscarinic), dopaminergic, histaminergic, or serotonergic receptors.

ABBREVIATIONS

CTZ	chemoreceptor triggering zone
NK-1	neurokinin-1 receptor antagonist
NNT	number needed to treat
NSAIDs	nonsteroidal anti-inflammatory drugs
PDNV	post-discharge nausea and vomiting
PONV	postoperative nausea and vomiting

MANAGEMENT OF PONV

Reduction in Baseline Risk Factors

Blanket use of PONV prophylaxis is not cost-effective and unnecessarily risks drug-related adverse effects. Most guidelines are in agreement that patients at low risk for PONV are unlikely to benefit from prophylaxis and that it should be reserved for patients at moderate to high risk. Patients with no more than one risk factor are considered low risk. Identifying patient risks remains a challenge.

Apfel et al.[13] devised a simplified risk score for predicting PONV. They concluded that there are 4 main risk factors:

1. female sex,
2. prior history of motion sickness or PONV,

3. non-smoker, and

4. the use of postoperative opioids.

The estimated probability of PONV was 10%, 21%, 39%, and 78% with 0, 1, 2, 3, and 4 risk factors, respectively.

Risk Factors for PONV

These can de divided into 3 main groups:

- **Patient-specific**: female sex[8,13]; non-smoker[13,14]; history of PONV or motion sickness.[13–15]
- **Anaesthetic**: use of volatile anaesthetics within 0 to 2 hours[16]; use of nitrous oxide[17]; use of intraoperative and postoperative opioids[13,18–21]; high doses of neostigmine.
- **Surgical**: duration of surgery, with each 30-minute increase in duration increasing the risk of PONV by 60%.[22]

Recommendation

1. Physicians should be aware of the risk factors associated with PONV, and the baseline risks should be reduced whenever possible. (III-A)

Optimization in the Perioperative Period

A number of perioperative factors have been shown to reduce the risk of PONV.

When possible, regional anaesthetic should be administered as general anaesthetic is associated with an 11-fold increased risk of PONV.[22] When general anaesthetic is required, the use of propofol as the induction agent is effective in reducing early PONV incidence when compared with other induction agents. The number needed to treat with propofol to reduce PONV is approximately 5.[23]

Avoidance of intraoperative and postoperative opioids has been shown to reduce PONV. Moiniche et al. showed that treatment with NSAIDs as compared with opioids decreased the risk of PONV.[20] The use of supplemental oxygen perioperatively has been shown to reduce PONV by 50%.[24,25] possibly by reducing gastrointestinal hypoxia. However, there is conflicting evidence, and a recent study by Turan et al. demonstrated no benefit associated with supplemental oxygen.[26]

Perioperative intravenous fluid administration has been shown to reduce PONV.[27,28] The mechanism is unclear but may be related to the release of serotonin due to decreased intestinal perfusion, which can be caused by the drop in systolic blood pressure seen with some induction agents.

Neostigmine, a reversal agent for non-depolarising muscle relaxants, is associated with increased PONV, especially in large doses (> 2.5 mg),[29] and should be avoided if possible.

Recommendations

2. When the choice is available, patients should be advised that the risk of PONV decreases when regional rather than general anaesthesia is administered. (III-A)

3. The perioperative use of opioids should be minimized. Surgeons should evaluate the risks/benefits of opioid administration in light of the increased risk of PONV. (III-B)

Pharmacological Prophylaxis

Prophylactic doses and timing for the administration of antiemetics are shown in Table 2.

Serotonin (5-HT_3) receptor antagonists exert their effects in the chemoreceptor trigger zone and at vagal afferents in the gastrointestinal tract. Ondansetron was the first of this class of drug to be marketed; others include dolasetron, tropisetron, and granisetron.

In 2003, an expert panel agreed that there was no evidence of any difference in the efficacy and safety profiles of the different 5-HT_3 receptor antagonists in the prophylaxis against PONV.[10] Ondansetron 4 mg has a NNT of 7 for the prevention of nausea and 6 for the prevention of vomiting. The number needed to harm with a single dose of ondansetron is 36 for headache, 31 for increased liver enzymes, and 23 for constipation.[30]

Dexamethasone, a corticosteroid, administered at a dose of 8–10 mg IV, prevents PONV with a NNT of 4.[38] Smaller doses of 2.5–5 mg have been shown to be as effective[13,40] The precise mode of action is not well understood, but may be due to the release of endorphins that elevate mood and stimulate appetite.[16] There are no reports of adverse effects in the doses used for the management of PONV.[38]

Droperidol blocks dopamine receptors in the CTZ. The efficacy of droperidol is equivalent to that of ondansetron, with a NNT of 5 for prevention of PONV. The FDA issued a "black box" warning about droperidol, stating that it may cause death associated with QT prolongation and torsades de pointes. In Canada, droperidol is still available but its use is limited by Health Canada.[48]

Metoclopramide blocks dopamine receptors in the CTZ and vomiting centre. It also shortens bowel transit time and in high doses blocks serotonin receptors. When used in standard clinical doses of 10 mg, metoclopramide was found to be ineffective for PONV prophylaxis.[49] A dose of 50 mg intravenous metoclopramide has been shown to significantly reduce late (> 12 hours) PONV, but the side effect profile is unsatisfactory.[47] The guidelines produced by Gan et al. do not recommend metoclopramide as a perioperative antiemetic.[10]

Dimenhydrinate, a commonly used antihistaminic, has similar efficacy to 5-HT_3 receptor antagonists.[43] Its efficacy is

Table 2. Prophylactic doses and timing for the administration of antiemetics

Drug	Dose	Timing	Adverse effects
Ondansetron	4–8 mg IV[30]	At end of surgery[31]	Headache, lightheadedness, elevated liver enzymes
Dolasetron	12.5 mg IV[32]	At end of surgery[32]	Headache, lightheadedness, elevated liver enzymes
Granisetron	0.35–1mg IV[33–35]	At end of surgery[33,35]	Headache, lightheadedness, elevated liver enzymes
Tropisetron	5 mg IV[36,37]	At end of surgery[36,37]	Headache, lightheadedness, elevated liver enzymes
Dexamethasone	5–10 mg IV[38–40]	Before induction[41]	Vaginal itching or anal irritation with IV bolus
Droperidol	0.625–1.25 mg IV[36,37]	At end of surgery[42]	Sedation, dizziness, anxiety, hypotension, EPS
Dimenhydrinate	1–2mg/kg IV[43]		Sedation, dry mouth, blurred vision, dizziness, urinary retention
Prochlorperazine	5–10mg IV[44]	At end of surgery[44]	Sedation, hypotension, EPS
Promethazine	12.5–25mg IV[44]	At end of surgery[44]	Sedation, hypotension, EPS
Scopolamine	Transdermal patch[45,46]	Prior evening or 4 hours before end of surgery[46]	Sedation, dry mouth, visual disturbances; CNS effects in elderly patients, renal or hepatic impairment
Metoclopramide	25 or 50 mg IV for prophylaxis[47]		Sedation, hypotension, EPS
Diclectin	10 mg doxylamine succinate and 10 mg pyridoxine hydrochloride	Before induction Prior evening, 2 tablets Before induction, morning of surgery, 1 tablet After surgery, 1 tablet	
Aprepitant	40 mg PO	1–3 hours prior to induction of anaesthesia	Headache, fatigue, dizziness elevated liver enzymes

presumably due to the high concentration of histamine and muscarinic cholinergic receptors within the vestibular system.[50]

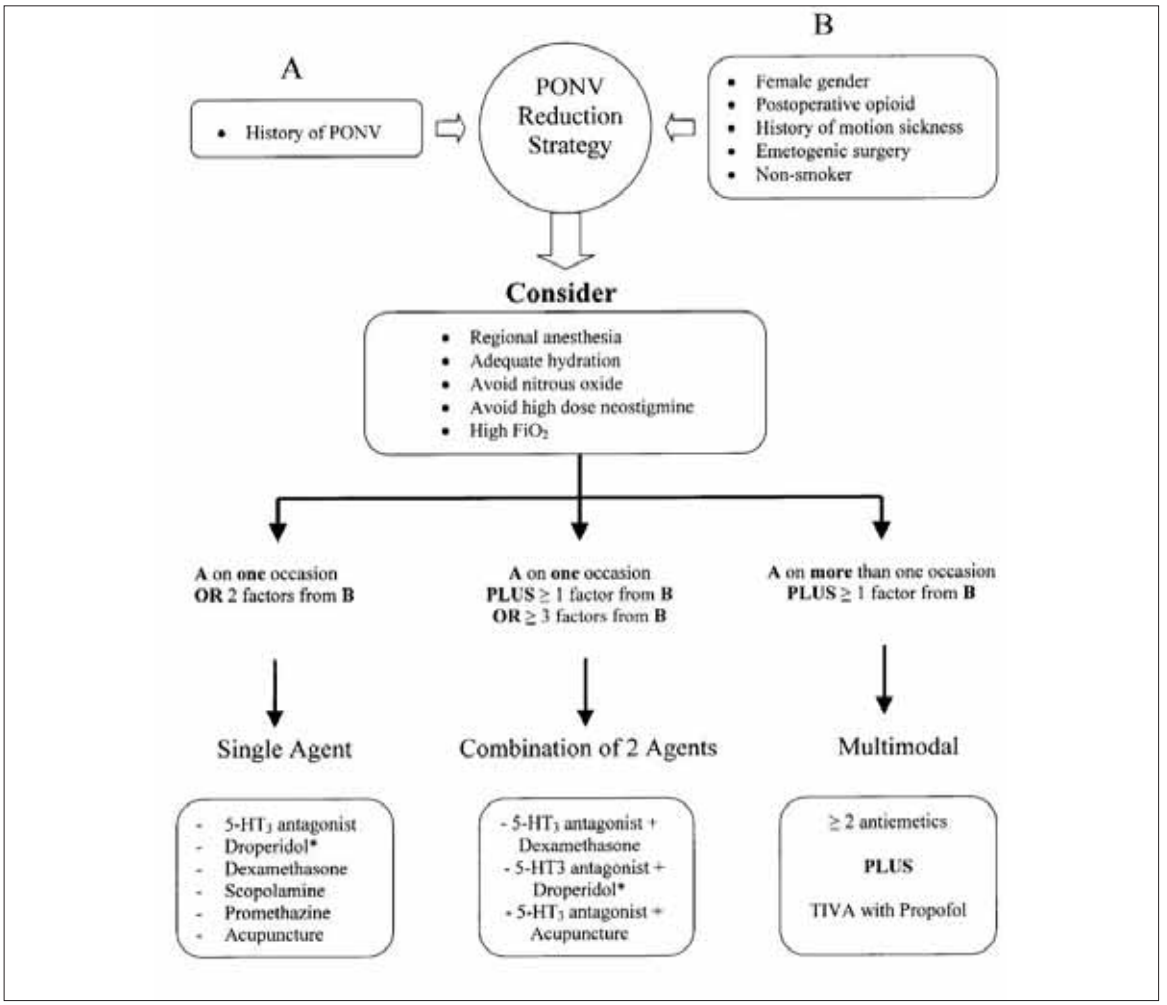
Promethazine and prochlorperazine belong to a group of drugs known as phenothiazines, which act primarily via a central antidopaminergic mechanism in the CTZ. The use of these drugs has decreased because of their significant side effects: sedation, dizziness, and extrapyramidal symptoms.

Scopolamine is an anticholinergic that blocks emetic muscarinic receptors in the cerebral cortex.[51] It is very effective, with a NNT of 3.8 for prevention of PONV.[52] Its use is limited because of its two- to four-hour onset of effect and side effect profile as listed above.

A recent publication has shown Diclectin to be as effective as ondansetron for the prevention of late postoperative vomiting in women undergoing laparoscopic tubal ligation, with an average NNT of 5.9.[53]

Diclectin is an antiemetic medication that contains 10 mg doxylamine succinate (a common antihistamine with antiemetic properties found in over-the-counter sleeping medication) and 10 mg pyridoxine hydrochloride (vitamin B6), in a delayed release formulation. Pyridoxine may have intrinsic antiemetic properties and also may be synergistic with the antinauseant property of antihistamines.[54–56] Diclectin has been used since the 1950s and is considered to be a safe treatment for nausea and vomiting associated with pregnancy.[57] The International Cochrane Collaboration has systematically reviewed randomized trials of Diclectin and concluded that it safely provides considerable relief for nausea and vomiting in pregnancy.[58]

Aprepitant was the first neurokinin-1 (NK-1) receptor antagonist approved for the treatment of PONV. This drug blocks NK1 receptors in the central and peripheral nervous systems thus preventing emesis. In one study, patients given oral aprepitant alone or in combination with intravenous ondansetron had significantly fewer emetic episodes than those given ondansetron alone.[59] In a report of combined data from 2 large trials, oral aprepitant 40 mg was superior to intravenous ondansetron 4 mg for the prevention of PONV.[60] Complete response (no nausea, vomiting, or need



for rescue therapy) was achieved in 37.9% of the aprepitant group compared with 31.2% of the ondansetron group. Its acquisition cost is relatively high, making it less appealing as a first line agent.

None of the available agents is entirely effective for preventing PONV, particularly for high-risk patients. As there are four major receptor systems involved in the etiology of PONV, a combination of agents that act on different receptors results in better prophylaxis.[61,62] The most commonly studied combinations have included 5-HT_3 receptor antagonists with droperidol or dexamethasone, and both are equally efficacious.[63,64] The Figure illustrates a proposed algorithm for the management of PONV

Recommendations

4. Prophylactic antiemetics should be administered to patients with moderate or high risk of developing PONV. (II-1 A)

5. In patients with a high risk of developing PONV, combination antiemetic therapy should be considered. (III-B)

Non-pharmacologic Prophylaxis

Acupuncture has been shown to be effective in the management of PONV. Coloma et al.[65] compared acustimulation with ondansetron for the treatment of established PONV in outpatient laparoscopic surgery patients. They concluded that acustimulation may be a satisfactory alternative to ondansetron for established PONV, and that ondansetron seems to enhance the efficacy of acustimulation for treatment of established PONV.

Ginger root is a commonly used non-medical therapy but is not effective for PONV prophylaxis.[66] Similarly, cannabinoids have not been confirmed to be effective in the management of PONV.

Recommendation

6. Acupoint electrical stimulation may be used as an alternative or adjuvant therapy for prevention of PONV. (II-1 A)

Rescue Treatment for PONV

In the presence of persistent nausea and vomiting, possible contributing factors, such as patient-controlled morphine analgesia, presence of blood in the pharynx, or an abdominal obstruction, should be excluded before rescue therapy may be initiated.

When prophylaxis with one drug has failed, a repeat dose of this drug should not be initiated as a rescue therapy. Instead a drug from a different class of antiemetics should be administered.[67] However, if the PONV occurs more than 6 hours after surgery, repeat dosing of the initial prophylactic drug may be considered. Repeat doses of dexamethasone and transdermal scopolamine should not be administered regardless of the time interval.[10]

If a patient has received no prophylaxis, treatment with a 5-HT_3 receptor antagonist may be considered.[68] Rescue treatment doses for 5-HT_3 receptor antagonists are approximately 25% the dose of those used for prophylaxis (e.g., 1 mg ondansetron).

Recommendations

7. For patients with PONV who did not receive prophylaxis or in whom prophylaxis failed, antiemetic treatment should be administered as soon as feasible. (III-A)
8. When prophylaxis with one drug has failed, a repeat dose of this drug should not be initiated as a rescue therapy; instead, a drug from a different class of antiemetic drugs should be administered. (III-A)

Post-discharge Nausea and Vomiting

PDNV is nausea and/or vomiting that occur after discharge from the health care facility, but within the 24-hour period immediately following surgery. Post-discharge nausea and vomiting that occurs after the initial 24-hour postoperative period is considered delayed PDNV.[69] Post-discharge nausea and vomiting is becoming more common as more patients are being operated on in an ambulatory setting, and it has been reported in 35% to 50% of patients.[70,71]

In a recent meta-analysis, the NNT to prevent post discharge nausea following ambulatory surgery was 12.9, 12.2, and 5.2 following the prophylactic administration of ondansetron 4 mg, dexamethasone, and a combination of two antiemetics, respectively. For post-discharge vomiting, the NNT was 13.8 for ondansetron 4 mg and 5 for combination treatment. These results suggest that ondansetron alone should not be used routinely in ambulatory patients at low risk and that patients at high risk are best managed with a combination strategy.[72]

Optimal management of PDNV is unsupported by scientific evidence, and the choice of medication for PDNV is left to the clinician.

In a study by Gan et al.[73] 4 mg IV ondansetron for PONV prophylaxis was administered. Patients were then randomized to receive either ondansetron oral disintegrating tablet (ODT) 8 mg or placebo immediately before discharge from the ambulatory surgery centre and again 12 hours later. Patients who received ondansetron ODT had less severe nausea and fewer vomiting episodes (3% vs. 23%) after discharge.

Al-Sadi et al.[74] assessed the efficacy of acupuncture as a prophylactic antiemetic. They found a significant difference between groups before and after discharge, with the placebo group four times more likely to have post-discharge nausea and vomiting than the acupuncture group.

Recommendations

9. As patients who undergo surgery in surgical daycare units may have PONV after they are discharged, they should be given instructions for its management. (III-B)
10. Patients at high risk of developing PDNV should be provided with rescue treatment. (III-B)

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