Evidence-based management of postoperative nausea and vomiting

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POSTOPERATIVE nausea and vomiting (PONV) is one of the most common complications following surgery. Prior to the 1960s, when older inhalational agents such as ether and cyclopropane were widely used, the incidence of vomiting was reported to be as high as 60%.^{1,2} Better anesthetic techniques, along with a new generation of antiemetics and shorter acting anesthetic drugs, reduced the incidence of PONV to about 30% in today's practice. Nevertheless, PONV still occurs, with an incidence as high as 60–70% in some high-risk patients.^{3,4} Pediatric populations are not spared from PONV. While the incidence may be lower in children less than two years of age,^{5,6} some procedures, tonsillectomies and strabismus surgery, are associated with high incidence of PONV.^{7,8} Ambulatory patients appear to have lower incidence of PONV compared with inpatients,⁹ but this could be related to the fact that post-discharge nausea and vomiting are not recognized. While PONV is rarely fatal, it is considered one of the most unpleasant postoperative symptoms. Even mild PONV may result in delayed hospital discharge, decreased patient satisfaction and increased use of resources, including medical and nursing care and other supplies.¹⁰ Avoiding PONV is very important to patients. They rated avoiding PONV more important than avoiding pain postoperatively.¹¹ Patients are willing to spend up to US \$100 out of their pocket for an effective antiemetic.¹²

Consensus guidelines on PONV management

The management of PONV is complex and there is literature supporting the use of every antiemetic available in practice. Hence, it is often difficult for practitioners to adopt an evidence-based practice for PONV management. Recently, a multidisciplinary panel of experts convened to review the medical literature on PONV and to produce guidelines for the management PONV.¹³ The panel consulted the med-

ical literature for level of evidence rating scales that were pertinent and widely used, then adapted them to the body of scientific literature relating to PONV.^{14,15} In the absence of published data, recommendations were made on the basis of expert opinion. The following scales were used in rating the guidelines:

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 aim of this 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 fall into level IV since such trials are not randomized. However, information emerging from that study may be judged as "A" by the panel.

Identification of patients at high risk for PONV enables targeting prophylaxis to those who will benefit most from it. Universal PONV prophylaxis is not cost effective, is unlikely to benefit patients at low risk for PONV and would put them at risk from the potential side effects of antiemetic agents. Patient, anesthesia, and

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surgery related risk factors have been identified (Guideline 1). Anesthesia related risk factors include the use of volatile agents, which cause PONV during the early postoperative period (within 0–2 hr),¹⁶ nitrous oxide,¹⁷ opioids^{3,16} and high doses of neostigmine (> 2.5 mg) for the reversal of neuromuscular blockade.¹⁵ Patient related factors include female gender,^{3,18} history of PONV or motion sickness^{3,18,19} and non-smoking status.^{3,19} High levels of anxiety and postoperative pain, especially of pelvic or visceral origin, may also be associated with a higher incidence of PONV.^{20–22}

According to a recent consensus panel, obesity and the stage of the menstrual cycle do not increase the risk of PONV.¹³ Long surgical procedures (each 30 min increase in duration increases PONV risk by about 60 %)¹⁸ and certain types of surgery also carry a greater risk of PONV.^{4,18,23} In adults, high incidences of PONV are found in intra-abdominal surgery, major gynecological surgery, laparoscopic surgery, breast surgery, neurosurgery, eye and otorhinolaryngology (ENT) surgery. Pediatric operations at high risk for PONV include strabismus, adenotonsillectomy, hernia repair, orchidopexy, penile surgery and middle ear procedures.^{24,25} Some authors, however, could not demonstrate an association between type of surgery and the risk of PONV.³ The incidence of PONV increases after the age of three years with a peak incidence of about 40% in the 11–14 yr age group.^{3,25,26} Prior to puberty, gender differences for PONV have not been identified.¹³

In a study of 2,722 patients, Apfel *et al.* developed a simplified risk score consisting of four predictors: female gender, history of motion sickness or PONV, non-smoking status and the use of opioids for postoperative analgesia. If none, one, two, three or four of these risk factors were present, the incidences of PONV were ten, 21, 39, 61 and 79% respectively.³

Guideline I. Identify adults at high risk for PONV

Patient-specific risk factors

- Female gender (IA)
- Non-smoking status (IVA)
- History of PONV/motion sickness (IVA)

Anesthetic risk factors

- Use of volatile anesthetics within zero to two hours (IA)
- Nitrous oxide (IIA)
- Use of intraoperative (IIA) and postoperative opioids (IVA)

Surgical risk factors

- Duration of surgery (each 30 min increase in duration increases PONV risk by 60%; IVA)
- Type of surgery (laparoscopy, ENT, neuro

surgery, breast, strabismus, laparotomy, plastic surgery; IVB)

Guideline II. Identify children at high risk for post-operative vomiting (POV)

Risk factors for POV in 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 high among children as among adults.
- Risk increases as children age, decreasing after puberty.
- Gender differences are not seen before puberty.
- Risk increases more consistently with specific operations.

Guideline III. Reduce baseline risk factors for PONV

Approaches for lowering baseline risk factors include:

- Use of regional anesthesia (IIIA)
- Use of propofol for induction and maintenance of anesthesia (IA)
- Use of intraoperative supplemental oxygen (IIIB)
- Use of hydration (IIIA)
- Avoidance of nitrous oxide (IIA)
- Avoidance of volatile anesthetics (IA)
- Minimization of intraoperative (IIA) and postoperative opioids (IVA)
- Minimization of neostigmine (IIA)

Guideline IV. Antiemetic therapy for PONV prophylaxis in adults

Serotonin (5-HT₃) antagonists

- Ondansetron (IA)
- Dolasetron (IA)
- Granisetron (IA)
- Tropisetron (IA)

Dexamethasone (IIA)

Droperidol (IA)

Dimenhydrinate (IIA)

Ephedrine (IIIB)

Prochlorperazine (IIIA)

Promethazine (IIIB)

Transdermal scopolamine (IIB)

Nonpharmacologic techniques

Acupuncture (IIA)

Hypnosis (IIIB)

Guideline V Antiemetic doses for children

Agent	Dose	Evidence
Ondansetron	50 – 100 µg·kg ⁻¹ up to 4 mg	IIA
Dolasetron	350 µg·kg ⁻¹ up to 12.5 mg	V

Dexamethasone	150 $\mu\text{g}\cdot\text{kg}^{-1}$ up to 8 mg	IA
Droperidol	50 – 75 $\mu\text{g}\cdot\text{kg}^{-1}$ up to 1.25 mg	IIA
Dimenhydrinate	0.5 $\text{mg}\cdot\text{kg}^{-1}$	IIA
Perphenazine	70 $\mu\text{g}\cdot\text{kg}^{-1}$	IA

Guideline VI Antiemetic treatment for patients with PONV who did not receive prophylaxis or in whom prophylaxis failed

Rule out inciting medication or mechanical causes of PONV (V)

Initial therapy

- No prophylaxis or dexamethasone
- 5-HT₃ antagonist* plus second agent**
- Triple therapy with 5-HT₃ antagonist* plus two other agents** when PONV occurs less than six hours postoperatively (in postanesthesia care unit; V)
- Triple therapy with 5-HT₃ antagonist* plus two other agents** when PONV occurs greater than six hours postoperatively (V)

Failed prophylaxis

- Administer low-dose 5-HT₃ antagonist* (IIA)
- Use agent from different class (V)
- Do not repeat initial therapy (IIIA)

Use agent from different class (V) or propofol, 20 mg *prn* (adults; IIIB)

- Repeat 5-HT₃ antagonist* and droperidol if last dose is greater than six hours (not dexamethasone or transdermal scopolamine)
- Use agent from different class (V)

*Low-dose 5-HT antagonist dosing: ondansetron 1.0 mg; dolasetron 12.5 mg; granisetron 0.1 mg; tropisetron 0.5 mg; **Alternative therapies for rescue: droperidol 0.5 mg *iv*; dexamethasone (2–4 mg *iv*); promethazine 12.5 mg *iv*.

Conclusion

While we have achieved significant advances in the management of PONV, it still occurs frequently in high-risk patients. 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 major risk factors for PONV are: female gender, non-smoking status, history of PONV/motion sickness, use of volatile anesthetics, nitrous oxide, intraoperative and postoperative opioids, increased duration of surgery, and type of surgery (laparoscopy, ENT, neurosurgery, breast, strabismus, laparotomy, plastic surgery).

The first step in reducing PONV risk is to reduce baseline risk factors among patients at risk (Figure).

FIGURE Algorithm for postoperative nausea and vomiting (PONV) prophylaxis.

There is increasing evidence that the combination of several potentially beneficial factors (multimodal approach) may lead to an improved outcome.

Drugs for PONV prophylaxis for adults include the 5-HT₃ antagonists: ondansetron, dolasetron, granisetron, and tropisetron; dexamethasone, droperidol, dimenhydrinate, transdermal scopolamine, ephedrine, prochlorperazine, and promethazine. These drugs should be considered for use as monotherapy or in combination for patients at moderate risk for PONV. In general, combinations are more effective than monotherapy. 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-HT₃ antagonist and a second drug. Antiemetic rescue therapy should be administered to patients who have an emetic episode after surgery. If PONV occurs within six hours postoperatively, patients should not receive a repeat dose of the prophylactic antiemetic. An emetic episode more than six hours postoperatively can be treated with any of the drugs used for prophylaxis except dexamethasone and transdermal scopolamine.

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