MANAGEMENT OF THE PATIENT AT HIGH RISK FOR POSTOPERATIVE NAUSEA AND VOMITING

ETHAN OLIVER BRYSON*, ELIZABETH A.M. FROST**
AND MEG ROSENBLATT***

Abstract

Postoperative nausea and vomiting continue to be problematic areas in anesthesia as evidenced by frequent reports of therapies in the literature. No single therapy has been proven curative for all cases, in part because of the several emetic centers, all of which may be blocked by different classes of drugs and the diverse risk factors which act alone or in combination to cause vomiting. Identification of the patient most at risk allows for cost effective prophylactic management. An appropriate anesthetic technique can be planned that, relying on evidence based medicine, will decrease if not prevent the incidence of this most troubling complication.

Introduction

The incidence of postoperative nausea and vomiting (PONV) is reported between 18% and 30% in most large series regardless of location or patient population but these figures include nausea without emesis and no distinction is made between mild and severe vomiting. The actual incidence of severe incapacitating vomiting remains steady, at about 0.1% to 0.6% of all anesthetics performed. Given the prevalence of PONV, the

From the Department of Anesthesiology, Mount Sinai Medical Center, New York, NY, USA.
* MD Senior Resident in Anesthesiology.
**MD Professor.
*** MD Associate Professor.
possibility that any patient could develop nausea and or vomiting requiring postoperative treatment, must be considered during preanesthetic assessment to allow development of a preemptive plan.

**Preanesthetic Assessment**

The preanesthetic interview should cover questions designed to determine the patient’s risk for developing PONV, and the anesthesiologist should consider the many variables (see Table 1) in formulating a perioperative plan. The overall risk that a particular patient will develop PONV depends upon factors unique to the patient, the surgical procedure, and the anesthetic technique.

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<table>
<thead>
<tr>
<th>Patient Factors</th>
<th>Surgical Factors</th>
<th>Anesthetic Factors</th>
</tr>
</thead>
<tbody>
<tr>
<td>● Age</td>
<td>● Type and area of surgery</td>
<td>● Use of nitrous oxide</td>
</tr>
<tr>
<td>● Gender</td>
<td>● Duration of procedure</td>
<td>● Use of potent inhaled agents</td>
</tr>
<tr>
<td>● Menstrual status</td>
<td></td>
<td>● Use of opioids</td>
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<tr>
<td>● Weight</td>
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<tr>
<td>● Smoking status</td>
<td></td>
<td></td>
</tr>
<tr>
<td>● History of PONV or motion sickness</td>
<td></td>
<td></td>
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<tr>
<td>● Fasting status</td>
<td></td>
<td></td>
</tr>
<tr>
<td>● Co-morbidities</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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**Patient Factors Associated with PONV**

Patient age has been shown to be a contributing factor in the development of PONV\(^3\) with children showing a greater propensity towards PONV. Among pediatric patients the incidence has been shown to be as high as 34% in the 6-10 year age group but considerably lower in younger patients, and the incidence decreases with the onset of puberty\(^4\). Geriatric patients have a much lower incidence.

In adult patients, gender has been shown to have a greater influence
on the development of PONV than age, with premenopausal women and
postmenopausal women less than 60 years of age, more susceptible than
men\textsuperscript{5}. This gender difference is not observed in the pediatric population
or in adults older than 60 years of age and consequently the etiology is
thought, by some, to involve variations in serum gonadotropins\textsuperscript{6}. Several
studies have noted differences in the incidence of PONV experienced by
women at different stages in the ovulatory cycle, with menstruation and
the pre-ovulatory phase increasing the risk\textsuperscript{6}. A premenopausal woman in
the immediate pre-menstrual phase of her cycle is at greater risk for
developing PONV than a male of the same age undergoing the same
procedure or, presumably a comparable female at a different stage in her
cycle.

Whether or not weight alone is an independent risk factor for the
development of PONV remains controversial. Several studies have
suggested that patient weight is associated with the risk for development
of PONV with obesity, defined by a body mass index (BMI) of greater
than 30, increasing the risk\textsuperscript{7}. A number of factors have been suggested as
to why this correlation exists, including the potential for air to be forced
into the stomach during the handling of a difficult airway, as may be
encountered in the obese patient, the larger percentage of body fat in
which fat soluble anesthetic agents can be stored and delayed gastric
emptying\textsuperscript{8}. More recently, however, a systematic review of available data
by Kranke et al suggests that BMI is not correlated with an increased risk
for the development of PONV\textsuperscript{9}. An increased BMI may increase the
incidence of PONV in patients with other independent risk factors. Body
mass index is calculated by dividing weight in kilograms by height in
meters squared.

A number of conditions that may or may not be related to the surgery
have been identified as risk factors. Patients deemed to have a “full
stomach” and who are not fasting are at greater risk of regurgitation.
Co morbidities such as gastroesophageal reflux disease, hiatal hernia, liver
disease, and gastroparesis with associated decreased gastric motility and
delayed gastric emptying are some examples\textsuperscript{10}. Gastroparesis and ileus are
commonly associated with opioid administration as part of an anesthetic
regimen but may also be secondary to diabetes mellitus or a number of other medical conditions, including scleroderma and amyloidosis. Anxiety is known to reduce the pH of gastric fluid and increase its volume, making the patient more likely to develop PONV but depression without associated anxiety has not been identified as a risk factor.

The patient factor most closely associated with an increased risk for developing PONV is a prior history of the complication or a propensity to motion sickness. These patients may have a well-developed vomiting reflex arc but the exact mechanism is unclear. Also, for reasons that are not understood, smoking, appears to confer a preventive effect.

**Surgical Factors Associated with PONV**

Some surgical procedures are more likely to cause PONV than others, even in patients not otherwise at risk, and independent of the anesthetic agents used. Surgical operations that have been linked to a higher incidence of PONV include gynecologic or general abdominal procedures, head and neck surgery, eye surgery, and laparoscopic procedures in general. The duration of surgical procedure also affects the incidence of PONV, independent of other factors, with a longer duration of procedure positively correlated with a greater likelihood of the development of PONV. Increasing the duration by 30 minutes may increase the risk of PONV by 60%.

**Anesthetic Factors Associated with PONV**

Nausea, vomiting and retching can occur after general or spinal and epidural anesthesia, peripheral nerve blocks, and even after monitored anesthesia care cases. While the patient and surgical factors noted above cannot be controlled by the anesthesiologist, there are a number of decisions that can be made and techniques employed to reduce the incidence of PONV in patients at risk. Factors under the control of the anesthesiologist are divided into preoperative, intraoperative, and postoperative factors.
Preoperative factors

Several agents used preoperatively have been shown to affect the incidence of PONV. Benzodiazepines such as midazolam, often used as premedication to reduce anxiety and produce amnesia, appear to decrease the incidence of PONV\textsuperscript{14}. A similar beneficial effect is seen when the alpha agonist clonidine is used for preoperative sedation\textsuperscript{15}. Premedication with opioids increases the incidence of PONV\textsuperscript{16} but when pain is a factor, the relief of pain pre-operatively is associated with less PONV\textsuperscript{3}. Agents used as preoperative vagolytics and antisialagogues such as atropine and glycopyrrolate have been associated with an increased incidence of PONV, but it appears that atropine may be considerably less emetogenic than glycopyrrolate\textsuperscript{17}. Agents such as metoclopramide, which promote gastric emptying, may result in a decreased incidence of PONV, likely due to decreased gastric volume\textsuperscript{17}.

Intraoperative agents

While the potent anesthetic agents used for the maintenance of general anesthesia today do not result in the near 100% rate of PONV observed with cyclopropane and ether, they are associated with an elevation in the incidence of PONV, with a direct correlation between length of exposure and dosage\textsuperscript{18}. Nitrous oxide increases PONV, and omission of this gas from the anesthetic regime, especially in patients at risk, significantly reduces episodes of PONV\textsuperscript{19}. All of the volatile anesthetic agents, however, have been shown to cause vomiting and there are no statistical differences between the emetogenicity of halothane, enflurane, isoflurane, sevoflurane, or desflurane, even when used at or below 1 MAC\textsuperscript{18}. The technique of pure inhaled anesthesia, using the potent inhaled agents with or without nitrous oxide and not supplementing with opioid analgesics, is less emetogenic than the more commonly used balance technique in which intravenous opioids combined with N\textsubscript{2}O are used, but is associated with a significantly higher incidence of PONV than total intravenous anesthesia (TIVA) with propofol and no N\textsubscript{2}O\textsuperscript{20}. When propofol is substituted for the inhaled
agents, the incidence of PONV is reduced by about 20%\(^{18}\).

Intravenous agents used intraoperatively have also been associated with PONV, both positively and negatively. Propofol has been shown to reduce the incidence of PONV when used for induction or maintenance of general anesthesia, though a single induction dose does not reduce the incidence of PONV if the case is long and propofol is not used for maintenance\(^{21}\). When etomidate or ketamine is used for induction of anesthesia an increase in the incidence of PONV is observed\(^{22}\), though the residual effects of ketamine may have a benefit in the reduction of postoperative pain and the reduced need for postoperative narcotics, both of which contribute to a decreased incidence of PONV\(^{23}\). Induction of general anesthesia with barbiturates such as sodium thiopental has not been shown to affect PONV but studies which looked at TIVA with barbiturates showed a level of PONV greater than that observed with propofol\(^{24}\). Reversal of residual neuromuscular blockade with cholinesterase inhibitors can increase the incidence of PONV\(^{25}\), however some studies have suggested that the emetic effect can be lessened by substituting atropine for glycopyrrolate\(^{26}\).

Management of the airway during positive pressure ventilation, either during induction and prior to intubation, or intraoperatively, such as might occur during mask ventilation or after placement of a Laryngeal Mask Airway\(^{\circ}\), can result in the distension of the stomach and increase the incidence of PONV. One study suggests that care of the airway by inexperienced persons increases the incidence of PONV\(^{27}\) while another study points out that the incidence of PONV may not be lessened by the routine emptying of gastric contents via an orogastric tube\(^{28}\), although this technique is commonly used at the end of a case in patients at high risk.

The use of regional anesthesia may reduce the incidence of PONV in patients at risk by avoiding general anesthesia and the need for opioids to control pain. When a long acting agent is used, significant postoperative analgesia can be provided with a single injection. The placement of an epidural or peripheral nerve catheter allows continuous infusion of a local anesthetic, extending the period of postoperative analgesia and reducing
or eliminating the need for systemic opioids. Opioids infused with the local anesthetic through the catheter are absorbed systemically and have the potential to contribute to PONV. Though considerably less likely to cause PONV, the techniques are not entirely without increased risk, and if the regional technique fails, general anesthesia may be necessary. Hypotension may result from neuraxial anesthesia with spinal and epidural placement and increase the incidence of nausea and vomiting, both intra and postoperatively. The impact of this vascular perturbation can be lessened by prehydration prior to neuraxial block and maintenance of blood pressure with vasoactive agents as necessary, or by using a peripheral nerve block when appropriate.

The technique of monitored anesthesia care, the use of local anesthesia with sedation and monitoring by an anesthesiologist, can be used for many procedures, and is associated with a decrease in the incidence of PONV, especially when propofol is used. If opioids are used as analgesic adjuncts, the incidence of PONV is increased, as would be expected. However, the use of nonsteroidal anti-inflammatory drugs (NSAIDs) such as ketorolac (Toradol®) can reduce the need for opioids and therefore avoid the increased incidence of PONV. Also, a multimodal approach combining reduced dosages of narcotics and NSAIDs allows potentiation of analgesic effect and decreased severity of complications from both groups.

Postoperative factors

Once the patient has emerged from anesthesia, a number of factors can influence the incidence of PONV. Postoperative pain and the method of pain control employed, dizziness and disorientation, early ambulation and oral intake, and hydration all play a role in determining the onset and severity of PONV.

Pain itself is emetogenic and a well recognized causative factor of PONV, but the treatment of postoperative pain with opioids can increase PONV, so much that some patients opt to forgo pain management to avoid the associated malaise. Direct stimulation of the chemoreceptor...
trigger zone and vestibular apparatus as well as the decreased gastric emptying and bowel atony caused by all opioids used for postoperative analgesia make selection of effective pain management difficult at best. Strategies that lessen the dose of opioids used such as patient controlled analgesia (PCA) and supplementation with non-narcotic analgesic agents are associated with a decreased risk. Patient controlled epidural anesthesia (PCEA) and continuous epidural nerve blocks which rely on local anesthetics alone, avoid the administration of emetogenic agents while also controlling postoperative pain. Yet another means to reduce the adverse gastrointestinal effects associated with the administration of opioids may come in the development of specific μ opioid receptor antagonists which do not cross the blood brain barrier and thus preserve the analgesic actions but prevent bowel atony. Such agents including methylnaltrexone and alvimopam are currently under investigation.

Residual anesthetic effects in the immediate postoperative period may contribute to dizziness and disorientation and increase the incidence of PONV, an effect exacerbated by hypovolemia, anemia, hypoxia, or opioids administered for postoperative pain control. Early ambulation or movement can trigger an episode of PONV and some anesthesiologists suggest that patients with a history of PONV should restrict their movements postoperatively if possible. Hypovolemia can be avoided with the liberal administration of fluids intraoperatively and such treatment has been shown to reduce the incidence of dizziness but has not been shown to affect the incidence of PONV. Many patients who develop PONV do so after their first postoperative oral intake; therefore it is not currently recommended to mandate that patients demonstrate ability to drink without vomiting before being discharged from the post-anesthesia care unit. However, there are studies suggesting that restricting oral intake does not reduce the incidence of PONV.

**Prevention and Treatment of PONV**

Despite the relatively high overall incidence of PONV, most afflicted patients have minimal nausea associated with a small number of
emetic episodes, so the routine use of antiemetic prophylaxis is neither indicated nor cost-effective. Commonly seen side effects of antiemetic prophylaxis range in severity from dry mouth, blurry vision, and headache to dysphoria, sedation, and extrapyramidal symptoms. Given the potential for harmful side effects if patients are treated empirically, a rationale for prophylactic care must be developed. Because patients at high risk for developing PONV are also at higher risk for developing intractable PONV requiring repeated doses of rescue medications and unplanned postoperative hospital admission, the risks of prophylaxis in this group are considerably less than the risks associated with no treatment. Since side effects from commonly used prophylactic agents can require intervention and result in a prolonged stay in the post anesthetic care unit or an unplanned hospital admission, it is up to the anesthesiologist to balance the risks of not administering antiemetic prophylaxis with any untoward effects and identify only those patients who will likely benefit from prophylactic administration.

Once it has been determined by the anesthesiologist that antiemetic prophylaxis will be administered, the choice of agent or combination of agents must be made (see Table 2). The antiemetic agents available work by different mechanisms at different receptor sites (Figure 1) and have different pharmacologic profiles and side effects (see Table 3).
Table 2
Agents Used for PONV Prophylaxis (*)

<table>
<thead>
<tr>
<th>Prophylaxis</th>
<th>Adult Dose</th>
<th>Timing of Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Promethazine 25 mg PO, PR</td>
<td>1 hour prior to induction</td>
<td></td>
</tr>
<tr>
<td>12.5-25 mg IV</td>
<td>at the end of surgery</td>
<td></td>
</tr>
<tr>
<td>Prochlorperazine 5-15 mg PO</td>
<td>1 hour prior to induction</td>
<td></td>
</tr>
<tr>
<td>5-10 mg IV</td>
<td>at the end of surgery</td>
<td></td>
</tr>
<tr>
<td>Chlorpromazine 10-25 mg PO</td>
<td>1 hour prior to induction</td>
<td></td>
</tr>
<tr>
<td>100 mg PR</td>
<td>1 hour prior to induction</td>
<td></td>
</tr>
<tr>
<td>Diphenhydramine 50 mg PO</td>
<td>1 hour prior to induction</td>
<td></td>
</tr>
<tr>
<td>10-50 mg IV</td>
<td>after induction</td>
<td></td>
</tr>
<tr>
<td>Hydroxyzine 25-100 mg IM</td>
<td>after induction</td>
<td></td>
</tr>
<tr>
<td>Cyclizine 50 mg IM</td>
<td>after induction</td>
<td></td>
</tr>
<tr>
<td>Scopolamine Patch 1.5 mg transdermal</td>
<td>applied morning of surgery</td>
<td></td>
</tr>
<tr>
<td>Metoclopramide 10-20 mg IV</td>
<td>after induction</td>
<td></td>
</tr>
<tr>
<td>Dexamethasone 5-10 mg IV</td>
<td>at the end of surgery</td>
<td></td>
</tr>
<tr>
<td>Trimethobenzamide 300 mg PO or</td>
<td>1 hour prior to induction</td>
<td></td>
</tr>
<tr>
<td>200 mg PR</td>
<td>1 hour prior to induction</td>
<td></td>
</tr>
<tr>
<td>200-250 mg IV</td>
<td>at the end of surgery</td>
<td></td>
</tr>
<tr>
<td>Ondansetron 8 mg PO (available as an orally disintegrating preparation)</td>
<td>1 hour prior to induction</td>
<td></td>
</tr>
<tr>
<td>4 mg IV</td>
<td>after induction</td>
<td></td>
</tr>
<tr>
<td>Granisetron 0.1-1.0 mg IV</td>
<td>at the end of surgery</td>
<td></td>
</tr>
<tr>
<td>Droperidol 0.625-1.25 mg IV</td>
<td>at the end of surgery</td>
<td></td>
</tr>
<tr>
<td>Dolasetron 100 mg PO</td>
<td>1 hour prior to induction</td>
<td></td>
</tr>
<tr>
<td>12.5 mg IV</td>
<td>at the end of surgery</td>
<td></td>
</tr>
</tbody>
</table>

(*) Dose ranges as per medication package inserts.
**Table 3**  
*Antiemetics by class with side effects* Adverse effects appear to be specific to the site of action.

Phenothiazines (promethazine, prochlorperazine, chlorperazine)
- Extrapyramidal effects
- Sedation
- Confusion
- Excitation

Butyrophenones (droperidol)
- Extrapyramidal effects
- Sedation
- Lethargy
- Agitation

Antihistamines (diphenhydramine, hydroxyzine, cyclizine)
- Sedation

Anticholnergies (scopolamine)
- Dry Mouth
- Sedation
- Dysphoria
- Confusion/Disorientation
- Hallucinations/Visual Disturbances

Benzamides (metoclopramide, trimethobenzamide)
- Extrapyramidal effects
- Dystonia

Serotonin Antagonists (ondansetron, granisetron, dolasetron, tropesitron)
- Headache
- Light-Headedness
- Dizziness
- Constipation

Should prophylactic therapy not be effective and breakthrough or opioid induced PONV occur, then further treatment is indicated, either by combination therapy or moving to a different class (Table 4).
Table 4
Agents Used in the Treatment of PONV(*)

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Adult Dose</th>
<th>Pediatric Dose</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Promethazine</td>
<td>12.5-25 mg IV</td>
<td>0.25-1 mg/kg PR</td>
<td>single dose</td>
</tr>
<tr>
<td>Prochlorperazine</td>
<td>5-10 mg IV</td>
<td>0.1 mg/kg PR</td>
<td>q12 hrs</td>
</tr>
<tr>
<td>Doperidol</td>
<td>0.625-1.25 mg IV</td>
<td>25-75 mcg/kg IV</td>
<td>single dose</td>
</tr>
<tr>
<td>Diphenhydramine</td>
<td>10-50 mg IV</td>
<td>1 mg/kg IV</td>
<td>q6-8 hrs</td>
</tr>
<tr>
<td>Hydroxyzine</td>
<td>25-100 mg IM</td>
<td>1 mg/kg IV, IM</td>
<td>q6 hrs</td>
</tr>
<tr>
<td>Cyclizine</td>
<td>50 mg IM</td>
<td>1 mg/kg IM</td>
<td>q4-6 hrs</td>
</tr>
<tr>
<td>Scopolamine</td>
<td>0.3-0.65 mg IV, IM</td>
<td>6 mcg/kg IV, IM, SC</td>
<td>q4-6 hrs</td>
</tr>
<tr>
<td>Metoclopramide</td>
<td>10-20 mg IV</td>
<td>0.1-0.25 mg/kg IV</td>
<td>q6 hrs</td>
</tr>
<tr>
<td>Trimethobenzamide</td>
<td>300 mg PO, IV</td>
<td>100 mg PR, PO</td>
<td>q6 hrs</td>
</tr>
<tr>
<td></td>
<td>200 mg PR</td>
<td>if &lt; 15 kg</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>200 mg PR, PO</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>if &gt; 15 kg</td>
<td></td>
</tr>
<tr>
<td>Ondansetron</td>
<td>1-4 mg IV</td>
<td>0.05-0.1 mg/kg IV</td>
<td>single dose</td>
</tr>
<tr>
<td>Granisetron</td>
<td>0.1-1.0 mg IV</td>
<td>40 mcg/kg IV</td>
<td>single dose</td>
</tr>
<tr>
<td>Dolasetron</td>
<td>12.5 mg IV or</td>
<td>0.35 mg/kg IV</td>
<td>single dose</td>
</tr>
<tr>
<td></td>
<td>100 mg PO</td>
<td>(up to 12.5 mg)</td>
<td></td>
</tr>
</tbody>
</table>

(*) Dose ranges and timing of doses as per package inserts.

Promethazine (Phenergan®), prochlorperazine (Compazine®), and chlorpromazine (Thorazine®) are all phenothiazines, thought to exert their antiemetic effects by directly acting on the central dopaminergic receptors of the chemoreceptor trigger zone3. These agents are most effective in the treatment of opioid induced PONV, but their use as the primary treatment for PONV is limited by their tendency to cause sedation. Also, these agents have a narrow therapeutic index, and confusion, excitation, and extrapyramidal effects occur at higher doses. One study suggests that preoperative treatment with a phenothiazine is as effective in preventing PONV as newer, more expensive agents, and that effective prophylaxis can be achieved with lower doses that are associated with fewer side effects38.
Droperidol (Inapsine®) is the only butyrophenone currently used in the treatment of PONV. Like the phenothiazines, droperidol acts competitively on central dopaminergic receptors and is associated with sedation, lethargy, agitation and extrapyramidal effects, but the incidence of the more serious side effects is lower. Excessive postoperative sedation is common when patients are given higher doses of droperidol, and in the past this complication has limited use in outpatient anesthesia. Recent studies have shown that lower doses are just as effective in the prevention and treatment of PONV and are associated with less postoperative sedation. The addition of a “black box” warning to the droperidol drug information sheet by the FDA has reduced the use of droperidol, an effective and safe prophylactic agent, to that of rescue agent for intractable cases of PONV. The concern is that, in some patients who receive droperidol, a prolonged QTc interval develops, putting these patients at risk to develop the ventricular arrhythmia, torsade de pointes. Despite the limited evidence that antiemetic doses trigger this arrhythmia, the “black box” warning requiring electrocardiographic monitoring remains part of the package insert.

Diphenhydramine (Benadryl®), hydroxyzine (Atarax®, Vistaril®), and cyclizine (Marezine®) are all antihistamines which work to prevent nausea and vomiting by acting on the H1 receptors. Use as postoperative agents is limited by the excessive sedation associated with administration. These agents are most effective in the control of emesis caused by vestibular stimulation as is seen in patients with motion sickness and after middle ear surgery. They are rarely effective as a single agent but are often combined with drugs such as the phenothiazines known to produce extrapyramidal effects in order to mitigate the severity of these side effects.

Scopolamine is an anticholinergic agent that acts on the muscarinic and histaminic receptors of the vestibular apparatus and the nucleus of the tractus solitarius to reduce the incidence of PONV. It has been found to be very effective in patients treated with opioids for post-operative pain control and after middle ear surgery, though use is limited by a high incidence of sedation and dry-mouth. Other troubling side effects
include dysphoria, confusion, disorientation, visual disturbances and hallucinations\(^3\). Some studies have suggested that the efficacy of scopolamine in the prevention of PONV is no more than that of placebo\(^{42}\), though recently scopolamine, in the form of a transdermal patch applied the evening before or the morning of surgery, has been shown to reduce the incidence of PONV as effectively as ondansetron\(^{43}\). The authors of this study reported effective PONV prophylaxis in a high risk patient population by applying the transdermal scopolamine patch the morning of surgery. The reduced incidence of PONV was achieved with an insignificant incidence of side effects such as dry mouth but at only 25% the cost of IV ondansetron incurred by this institution.

Metoclopramide and trimethobenzamide are benzamides that act on both central dopamine and serotonin receptors, with both prokinetic and antiemetic effects. Metoclopramide increases gastrointestinal tract motility, decreasing gastric emptying time and gastric volume, and is usually well tolerated in adult patients. Side effects seen in this class of agents include extrapyramidal effects and dystonia, though these actions are more often seen in the pediatric population. Unlike the other agents discussed above, metoclopramide is not associated with sedation, making it a more attractive agent for outpatient treatment or prophylaxis. However, some studies have suggested that metoclopramide is considerably less effective than other agents, sedating or not, in the treatment of established PONV\(^{44}\).

Ondansetron, granisetron, dolasetron, tropisetron and other serotonin antagonists have been shown to provide effective treatment and prophylaxis of PONV and are associated with a low incidence of mild side effects\(^{44}\). These agents are not dopamine, muscarinic or histamine receptor antagonists, and, as such, are not associated with the side effects common to those classes. Side effects common to the serotonin antagonists include headache, light-headedness, dizziness and constipation. In one study, preoperative ondansetron was shown to be as useful as droperidol in the prevention and treatment of PONV, though less cost effective considering that the administration of droperidol was not associated with an increased length of stay or other adverse side
Granisetron has also been shown to effectively reduce the incidence of PONV in patients at risk, including pediatric patients and menstruating women. Agents that do not act directly on receptors known to be involved with emetogenesis may be effective in reducing the incidence of PONV indirectly by mitigating symptoms known to be emetogenic. Anxiolytics such as midazolam, for example, may effectively reduce the nausea and vomiting that commonly accompanies anxiety. Agents which reduce the need for opioids, as discussed previously, can be used as prophylaxis in patients at risk for PONV. Ephedrine and other agents that help maintain blood pressure may be used to prevent the nausea associated with hypotension postoperatively.

The use of single dose steroids as prophylaxis for the prevention of PONV has become commonplace in many institutions. Dexamethasone, previously used in combination therapy, has been shown to reduce the incidence of PONV when used as the sole agent, and is now frequently used as such. Several studies have examined the efficacy of this agent in the context of different types of surgical procedures. A recent randomized clinical trial found a significant decrease in the incidence of PONV after laparoscopic cholecystectomy when dexamethasone was administered preoperatively as the sole antiemetic agent. Patients receiving dexamethasone in this study reported no more adverse events than those who received a placebo, and patients in the dexamethasone group who did develop PONV were significantly less likely to require rescue antiemetics.

When used as the sole antiemetic agent for women undergoing laparoscopic gynecological surgery, dexamethasone was shown to reduce the incidence of PONV significantly. The authors of this study concluded that, given its availability, low cost and few side-effects, dexamethasone should be more frequently used as the prophylactic antiemetic in women undergoing gynecologic laparoscopic surgery.

Since pharmacologic interventions have been unable to eliminate PONV, investigators have looked into the potential benefits of nonpharmacologic interventions. In one randomized, prospective, double-
blind and placebo-controlled study, the K-D2 point (the Korean hand acupressure point in Koryo Hand Therapy) was evaluated for efficacy in the prevention of postoperative nausea and vomiting. Placement of capsaicin ointment on the K-D2 point of both hands 1 h before laparoscopic cholecystectomy resulted in a significantly lower incidence of PONV, and the need for rescue anti-emetic treatment was also lower. Stimulation of the P6 acupressure point has been associated with decreased postoperative nausea and vomiting in high risk women and has also been shown to increase patient tolerance to experimental nauseogenic stimuli, as well as reducing the number of symptoms experienced.

The combination of antiemetic agents has been shown to significantly reduce the incidence of PONV in patients at risk, below that which is seen with any one agent alone. Combination therapy is most cost-effective for patients at high risk for the development of PONV and medium risk patients are often successfully treated with a single agent.

A summary of strategies is demonstrated in Table 5. It is interesting to note that in one survey patients were willing to pay $100.00 out of pocket to prevent PONV. Seventy six percent felt that avoiding PONV was important. The cost of a single incidence of postoperative vomiting has been calculated to exceed $300.00. While dexamethasone and droperidol are the least expensive of the antiemetics, single doses of the serotonin antagonists are usually less than $20.00.

Table 5
Anesthetic Strategies to Reduce the Incidence of PONV in Patients at Risk

- Pre-medicate as needed to reduce anxiety
- Pre-hydrate to avoid hypotension
- Avoid nitrous oxide and potent inhaled agents when possible
- Choose regional techniques when possible
- Use propofol for induction and maintenance of anesthesia
- Use agents that reduce the need for opioids
- Administer combination antiemetic prophylaxis prophylactically and intraoperatively
Management of a High Risk Case

A 30 year old lady presented for laparoscopic tubal ligation and possibly oophorectomy. She gave a history of prolonged vomiting after an ovarian cystectomy 1 year ago which required an extra 3 days of hospitalization. She had a BMI of 34 and was a non smoker. Her history was significant for anxiety and depression and both her parents were diabetic.

The decision was made to proceed with a spinal technique, thus avoiding the agents associated with general anesthesia that are known to increase the incidence of PONV. The patient was premedicated with 2 mg of midazolam and 10 mg of metoclopramide. One liter of fluid was administered prior to placing the neuraxial block. The patient received 10 mg dexamethasone and 4 mg ondansetron immediately after placement of the regional anesthetic and positioning was completed. Blood pressure was checked every 2 minutes in order to recognize and treat hypotension quickly. The intraoperative course was uncomplicated. Food and water were withheld until the patient felt a need to drink and asked for oral intake. The intravenous cannula was left in place until shortly before discharge the same evening. Pain was managed with ketorolac (Torodol®) 30 mg IV initially and later with acetaminophen orally. On follow-up 24 hours later the patient reported no symptoms of PONV. While one should never promise a patient an emesis free course, it is often possible to prevent a repeat of a previous unpleasant experience.

Summary

The anesthesiologist is charged with both the prevention and treatment of PONV. While fully one third of patients will develop PONV, this manifests itself in the form of one or two episodes of emesis associated with nausea, and the incidence of intractable PONV is less than 1%. Prophylaxis for PONV is neither cost-effective nor indicated for low risk patients, and most medium risk patients can be effectively treated with a single agent. When administering an anesthetic to a patient at high
risk for developing PONV, the plan should include pre-medication to reduce anxiety, agents that reduce the need for intraoperative and postoperative opioids, and the use of regional anesthetic techniques whenever possible. If general anesthesia cannot be avoided, agents such as propofol for induction and maintenance of anesthesia should be used to avoid or reduce the need for nitrous oxide and the potent inhaled agents. A combination of antiemetic prophylactic agents should be administered to those judged to be at high risk for developing PONV, and adequate intravenous therapy should avoid dehydration and hypotension postoperatively.
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