Lesson 251: PreAnesthetic Assessment of the Patient With a History Of Prolonged Postoperative Nausea and Vomiting

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DISCLOSURE STATEMENT  
The author and reviewer have no relationships with pharmaceutical companies or manufacturers of products to disclose. This educational activity may contain discussion of published and/or investigational uses of agents for the treatment of disease. Some uses of these agents have not been approved by the US Food and Drug Administration. Please refer to the official prescribing information for each product for approved indications, contraindications, and warnings.

LEARNING OBJECTIVES  
At the end of this activity, the participant should be able to:  
1. Cite the incidence of postoperative nausea and vomiting (PONV).  
2. Identify risk factors for PONV.  
3. List the commonly used antiemetic agents and discuss their efficacies.  
4. Describe a rationale for antiemetic prophylaxis.  
5. Explain the side effects of commonly used antiemetics.  
6. Outline the treatment of PONV.  
7. Recommend an antiemetic agent for prophylaxis based on its safety profile and cost.  
8. Design an appropriate anesthetic plan to reduce risks based on the patient and the surgical procedure.  
9. Present a treatment regimen for breakthrough PONV.  
10. Identify anesthetic techniques that should be avoided in patients with a history of severe PONV.

The incidence of postoperative nausea and vomiting (PONV) is reported to be between 18% and 30% in most large series, regardless of the location or patient population. However, these figures include nausea without vomiting, 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 cases in which anesthetics are administered. Given the prevalence of PONV and the possibility of any patient experiencing nausea or vomiting that requires postoperative treatment must be considered during the preanesthetic assessment to allow the development of a preemptive plan. The preanesthetic interview should cover questions designed to determine the patient’s risk for PONV, and the anesthesiologist should consider the many variables involved when formulating a perioperative plan (Table 1, page 42). The overall risk that PONV will develop in a particular patient depends on factors unique to the patient, surgical procedure, and anesthetic technique.

Patient Factors Associated With PONV  
The patient’s age has been shown to be a contributing factor in the development of PONV. Children have a greater propensity; among pediatric patients, the incidence has been shown to be as high as 34% in 6- to 10-year-olds, but considerably lower in younger children. The incidence of PONV decreases in children at the onset of puberty, and the incidence in geriatric patients is much lower. Our patient is 30 years old, and her age is not, in itself, an independent risk factor for the development of PONV, although her risk is higher than what would be expected for an age-matched male patient.

In adult patients, gender has been shown to have a greater influence on the development of PONV than has age, with premenopausal women and postmenopausal women younger than 60 years old more susceptible than men. This gender difference is not observed in the pediatric population or in adults older than 60 years, and consequently the etiology of PONV is thought, by some, to involve variations in serum gonadotropin levels. A number of studies have noted differences in the incidence of PONV in women at different stages of the ovulatory cycle, with menstruation and the preovulatory phase associated with an increased risk. Our patient is a premenopausal woman in the premenstrual phase of her cycle, which puts her at greater risk for PONV than a man of the same age undergoing the same procedure or, presumably, a woman of comparable age at a different stage of her cycle.

Whether increased weight alone is an independent risk factor for PONV remains controversial. Several studies have indicated that patient weight is correlated with risk for PONV; obesity (defined as a body mass index [BMI] >30) increases the risk. A number of reasons have been suggested for this correlation, including the following: the potential for air to be forced into the stomach during the...
A similar beneficial effect is seen when the 300 mg PO or 200 mg PR after induction 25 mg PO, PR.

Agents used preoperatively

**Adult Dose**

<table>
<thead>
<tr>
<th><strong>Prophylactic Agent</strong></th>
<th><strong>Adult Dose</strong></th>
<th><strong>Timing of Dose</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Chlorpromazine</td>
<td>10-25 mg PO</td>
<td>1 h before induction</td>
</tr>
<tr>
<td></td>
<td>100 mg PR</td>
<td>1 h before induction</td>
</tr>
<tr>
<td>Cyclizine</td>
<td>50 mg IM</td>
<td>after induction</td>
</tr>
<tr>
<td>Dexamethasone</td>
<td>5-10 mg I.V.</td>
<td>at end of surgery</td>
</tr>
<tr>
<td>Diphenhydramine</td>
<td>50 mg PO</td>
<td>1 h before induction</td>
</tr>
<tr>
<td></td>
<td>10-50 mg I.V.</td>
<td>after induction</td>
</tr>
<tr>
<td>Dolasetron</td>
<td>100 mg PO</td>
<td>1 h before induction</td>
</tr>
<tr>
<td></td>
<td>12.5 mg I.V.</td>
<td>at end of surgery</td>
</tr>
<tr>
<td>Droperidol</td>
<td>0.625-1.25 mg I.V.</td>
<td>at end of surgery</td>
</tr>
<tr>
<td>Granisetron</td>
<td>0.1-1.0 mg I.V.</td>
<td>at end of surgery</td>
</tr>
<tr>
<td>Hydroxyzine</td>
<td>25-100 mg IM</td>
<td>after induction</td>
</tr>
<tr>
<td>Metoclopramide</td>
<td>10-20 mg I.V.</td>
<td>after induction</td>
</tr>
<tr>
<td>Ondansetron</td>
<td>8 mg PO (available as an orally disintegrating preparation)</td>
<td>1 h before induction</td>
</tr>
<tr>
<td></td>
<td>4 mg I.V.</td>
<td>after induction</td>
</tr>
<tr>
<td>Prochlorperazine</td>
<td>5-15 mg PO</td>
<td>1 h before induction</td>
</tr>
<tr>
<td>Promethazine</td>
<td>25 mg PO, PR</td>
<td>1 h before induction</td>
</tr>
<tr>
<td></td>
<td>12.5-25 mg I.V.</td>
<td>at end of surgery</td>
</tr>
<tr>
<td>Scopolamine patch</td>
<td>1.5 mg transdermally</td>
<td>applied morning of surgery</td>
</tr>
<tr>
<td>Trimethobenzamide</td>
<td>300 mg PO or 200 mg PR</td>
<td>1 h before induction</td>
</tr>
<tr>
<td></td>
<td>200-250 mg I.V.</td>
<td>at end of surgery</td>
</tr>
</tbody>
</table>

*Dose ranges as per medication package inserts.*

**Intraoperative Agents**

Although the potent anesthetic agents used to maintain general anesthesia today do not result in the nearly 100% rate of PONV that was observed with cyclopropane and ether, they are nevertheless associated with an elevated incidence of PONV that is directly correlated with length of exposure and dose. Nitrous oxide (N₂O) increases PONV; omission of this gas from the anesthetic regimen, especially in patients at risk, significantly reduces episodes of PONV. All of the volatile anesthetic agents, however, have been shown to be emetogenic. There are no statistical differences between the emetogenicity of halothane, enflurane, isoflurane, sevoflurane, and desflurane, even when used at or below 1 minute alveolar concentration (MAC). The technique of pure inhaled anesthetic, in which the potent inhaled agents are administered with or without N₂O and are not supplemented with opioid analgesics, is less emetogenic than the more commonly used balanced technique, in which intravenous (I.V.) opioids are combined with N₂O. However, the pure inhaled anesthetic technique is associated with a significantly higher incidence of PONV than is total I.V. anesthesia with propofol and without N₂O. When propofol is substituted for the inhaled agents, the incidence of PONV is reduced by about 20%. The I.V. agents used intraoperatively have also been correlated 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. However, a single induction dose does not reduce the incidence of PONV if the case is long and propofol is not used for maintenance. When etomidate or ketamine is used for induction of anesthesia, the incidence of PONV is increased. The residual effects of ketamine may be beneficial, however, by reducing postoperative pain and the need for postoperative narcotics—thus contributing to a

**Surgical Factors Associated With PONV**

Some surgical procedures are more likely to cause PONV than others, even in patients not otherwise at risk, and independently of the anesthetic agents used. Surgical operations that have been linked to a higher incidence of PONV include gynecologic and general abdominal procedures, head and neck surgery, eye surgery, and laparoscopic procedures in general.

**Anesthetic Factors Associated With PONV**

Nausea, vomiting, andretching may occur after general anesthesia, spinal or epidural anesthesia, peripheral nerve blocks, and even monitored anesthesia care. Although the patient and surgical factors previously noted cannot be controlled by the anesthesiologist, a number of decisions can be made and techniques employed to reduce the incidence of PONV in patients at risk. Factors under the control of the anesthesiologist can be classified as preoperative, intraoperative, or postoperative.

**Preoperative Agents**

Several agents used preoperatively have been shown to affect the incidence of PONV. Benzodiazepines—such as midazolam, which is often used as premedication to reduce anxiety and produce amnesia—appear to decrease the incidence of PONV. A similar beneficial effect is seen when the ß-agonist clonidine is used for preoperative sedation. Premedication with opioids increases the incidence of PONV, but when pain is a factor, the relief of pain preoperatively is associated with a decrease in PONV. Agents used preoperatively as vagolytics and antialisialogues, 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. The use of agents, such as metoclopramide, that promote gastric emptying may decrease the incidence of PONV, likely because of the decrease in gastric volume.

**Table 1. Factors Related to Risk for PONV**

<table>
<thead>
<tr>
<th>Patient factors</th>
<th>Environmental factors</th>
<th>Surgical factors</th>
<th>Other factors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>Environment</td>
<td>Type and area of surgery</td>
<td>Age</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td>Duration of procedure</td>
<td>Smoking status</td>
</tr>
<tr>
<td>Menstrual status</td>
<td></td>
<td>Comorbidities</td>
<td>Age</td>
</tr>
<tr>
<td>Weight</td>
<td></td>
<td></td>
<td>Smoking</td>
</tr>
<tr>
<td>Smoking status</td>
<td></td>
<td></td>
<td>Smoking status</td>
</tr>
<tr>
<td>History of PONV</td>
<td></td>
<td></td>
<td>Smoking status</td>
</tr>
<tr>
<td>or motion sickness</td>
<td></td>
<td></td>
<td>Smoking status</td>
</tr>
<tr>
<td>Fasting status</td>
<td></td>
<td></td>
<td>Fasting status</td>
</tr>
<tr>
<td>Comorbidities</td>
<td></td>
<td></td>
<td>Comorbidities</td>
</tr>
</tbody>
</table>

**Table 2. Pharmacologic Agents for the Prophylaxis of PONV**

handling of a difficult airway, as may be encountered in an obese patient; a relatively large percentage of body fat in which fat-soluble anesthetic agents can be stored; and delayed gastric emptying. More recently, however, a systematic review of available data by Kraneo et al suggested that a high BMI is not correlated with an increased risk for PONV. A high BMI may increase the incidence of PONV in patients with other independent risk factors. The BMI is calculated by dividing weight in kilograms by the square of the height in meters. Our patient has a weight of 75 kg and a height of 1.63 m, giving her a BMI of 28. A BMI >25 and <30 is considered overweight, so our patient does not have an increased risk for PONV based on her weight alone.

A number of conditions that may or may not be related to the need for surgery have also been identified as risk factors. Patients deemed to have a “full stomach” and who are not fasting are at greater risk for regurgitation. Comorbidities such as gastroesophageal reflux disease, hiatal hernia, liver disease, and gastroparesis with associated decreased gastric motility and delayed gastric emptying are some examples. Gastroparesis and ileus are commonly associated with the administration of opioids as part of an anesthetic regimen, but they also may be secondary to diabetes mellitus or a number of other medical conditions, including scleroderma and amyloidosis. Although anxiety, which is known to reduce the pH of gastric fluid and increase its volume, can increase the likelihood that PONV will develop, the vomiting reflex arc, but the exact mechanism is unclear. Also, factors such as midazolam, which is often used as premedication to reduce anxiety and produce amnesia—appear to decrease the incidence of PONV. A similar beneficial effect is seen when the ß-agonist clonidine is used for preoperative sedation. Premedication with opioids increases the incidence of PONV, but when pain is a factor, the relief of pain preoperatively is associated with a decrease in PONV. Agents used preoperatively as vagolytics and antialisialogues, 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. The use of agents, such as metoclopramide, that promote gastric emptying may decrease the incidence of PONV, likely because of the decrease in gastric volume.

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The CME lesson is available online at www.mssm.procampus.net.

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**Image 37x911 to 784x961**

*IM, intramuscular; I.V., intravenous; PO, per os; PR, per rectum.*

**Surgical Factors Associated With PONV**

Some surgical procedures are more likely to cause PONV than others, even in patients not otherwise at risk, and independently of the anesthetic agents used. Surgical operations that have been linked to a higher incidence of PONV include gynecologic and general abdominal procedures, head and neck surgery, eye surgery, and laparoscopic procedures in general.
decreased incidence of PONV.23 The induction of general anesthesia with barbiturates such as sodium thiopental has not been shown to affect the occurrence of PONV, but studies that evaluated total i.v. anesthesia with barbiturates showed a level of PONV higher than that observed with propofol.24 The 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 before intubation, or intraoperatively such as during mask ventilation or after placement of a supraglottic laryngeal mask—can distend the stomach and increase the incidence of PONV. One study has suggested that care of the airway by inexperienced persons increases the incidence of PONV.27 Another study concluded 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 cases in high-risk patients.

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. Significant postoperative analgesia can be provided with a single injection when a long-acting agent is used. The placement of an epidural or peripheral nerve catheter allows the continuous infusion of a local anesthetic, which extends the period of postoperative analgesia and reduces or eliminates the need for systemic opioids. Opioids infused with a local anesthetic through a catheter are absorbed systemically and have the potential to contribute to PONV. Although considerably less likely to cause PONV, these techniques are not entirely without risk; if the regional technique fails, general anesthesia may be necessary.29 Neuraxial anesthesia with spinal and epidural placement may result in hypotension and increase the incidence of nausea and vomiting—both intraoperatively and postoperatively. The effect of such vascular perturbation can be lessened by hydrating the patient before the neuraxial block is administered, in addition to maintaining the blood pressure with vasoactive agents as necessary or using a peripheral nerve block when appropriate.30

The technique of monitored anesthesia care (the use of local anesthesia with sedation and monitoring by an anesthesiologist) can be implemented for many procedures and is associated with a decreased incidence of PONV, especially when propofol is used.31 When opioids are given as analgesic adjuncts, the incidence of PONV is increased, as would be expected. However, the use of nonsteroidal anti-inflammatory drugs, such as ketorolac, can reduce the need for opioids and therefore avoid an increased incidence of PONV. Also, a multimodal approach that combines reduced doses of opioids and nonsteroidal anti-inflammatory drugs potentiates the anesthetic effect and decreases the severity of complications of both classes of drugs.

Postoperative Factors

After the patient has emerged from anesthesia, a number of factors can influence the development of PONV. The degree of postoperative pain and the method of pain control that is 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 cause of PONV.3 However, the treatment of postoperative pain with opioids can increase PONV, so much so that some patients opt to forgo pain management to avoid the associated malaise.32 Direct stimulation of the chemoreceptor trigger zone and vestibular apparatus, in addition to the decreased gastric emptying and bowel atony caused by all operations or postoperative analgesia, make effective pain management difficult at best. Strategies such as patient-controlled analgesia, which lesens the dose of opioids used, and supplementation with nonopioid analgesic agents are associated with a decreased risk.33 Palivizumab (an epidual anesthetic and continuous epidural nerve blocks, which rely on local anesthetics alone, avoid the administration of emetogenic agents while controlling postoperative pain.

Another means for reducing the adverse gastrointestinal effects associated with opioids may become available with the development of specific µ-opioid–receptor antagonists that do not cross the blood–brain barrier and thus preserve analgesia while preventing bowel atony. Such agents, including systemically administered and alvimopan, are currently under clinical investigation.

Residual anesthetic effects in the immediate postoperative period may contribute to dizziness and disorientation and increase the incidence of PONV—effects that are exacerbated by hypovolemia, anemia, hypoxia, or the administration of opioids for postoperative pain control.34 Early ambulation or movement can also trigger an episode of PONV. Some anesthesiologists have suggested that in patients with a history of PONV, postoperative movement should be restricted if possible.35 Hypovolemia can be avoided with the liberal intraoperative administration of fluids. Such treatment has been shown to reduce the incidence of dizziness, but not to affect the incidence of PONV.36

In many patients in whom PONV develops, the problem arises after their first postoperative oral intake; therefore, it is not currently recommended that patients be required to demonstrate an ability to drink without vomiting before being discharged from the postanesthesia care unit. However, some studies suggest that restricting oral intake does not reduce the incidence of PONV.37

Prevention and Treatment of PONV

Despite the relatively high overall incidence of PONV, most afflicted patients experience minimal nausea associated with a small number of emetic episodes; thus, the routine use of antiemetic prophylaxis is neither indicated nor cost-effective.38 Common side effects of antiemetic prophylaxis range from dry mouth, blurry vision, and headache to dizziness, 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 PONV are also at high risk for the development of intractable PONV that requires repeated doses of rescue medication and an unplanned postoperative hospital admission, the risks associated with prophylaxis in this group are considerably less than the risks associated with no treatment.39 Because the side effects of commonly used prophylactic agents can require intervention and result in a prolonged stay in the postanesthesia care unit or an unplanned hospital admission, it is up to the anesthesiologist to balance the risk of not administering antiemetic prophylaxis against that of untoward effects. Only those patients who are identified as likely to benefit from the administration of prophylactic agents should receive them.

Once the anesthesiologist determines that antiemetic prophylaxis will be administered, the agent or combination of agents must be chosen (Table 2). Currently available antiemetic agents have different mechanisms of action at different receptor sites (Figure), along with different pharmacologic profiles and side effects (Table 3).

If prophylactic therapy is ineffective and breakthrough or opioid-induced PONV occurs, then further treatment is indicated—with either combination therapy or an agent from a different class (Table 4, page 44). A small number of antiemetic agents are believed to exert antiemetic effects by directly acting on the central dopaminergic receptors of the chemoreceptor trigger zone.3 These agents are most effective for treating opioid-induced PONV, but their use as a primary treatment is limited by their tendency to cause sedation. Also, they have a narrow therapeutic index; confusion, excitation, and extrapyramidal effects occur at higher doses. A study by Desilva and colleagues39 has suggested that prophylactic treatment with a phonotheazine is as effective in preventing PONV as treatment with newer, more expensive agents, and that effective prophylaxis can be achieved with lower doses that are associated with fewer side effects.

Droperidol 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; however, the incidence of the more serious side effects associated with droperidol appears to be specific to the site of action.

Table 3. Side Effects of Antiemetic Agents by Class*

<table>
<thead>
<tr>
<th>Class</th>
<th>Side Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anticholinergic</td>
<td>Sedation, dry mouth, dysphoria, confusion/disorientation, hallucinations/visual disturbances</td>
</tr>
<tr>
<td>Antihistamines</td>
<td>Sedation, dry mouth, dizziness, rash, headache</td>
</tr>
<tr>
<td>Benzamides</td>
<td>Sedation, dry mouth, dizziness, headache</td>
</tr>
<tr>
<td>Butyrophenone</td>
<td>Extrapyramidal effects, sedation, light-headedness, confusion, excitation</td>
</tr>
<tr>
<td>Phentothazine</td>
<td>Extrapyramidal effects, sedation, light-headedness, confusion, dizziness, constipation</td>
</tr>
<tr>
<td>Serotonin antagonists</td>
<td>Headache, light-headedness, dizziness, constipation</td>
</tr>
</tbody>
</table>

*Adverse effects appear to be specific to the site of action.

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CME

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Lesson 25 1

Lesson 25 1
Table 4. Pharmacologic Agents for the Treatment of PONV

<table>
<thead>
<tr>
<th>Agent</th>
<th>Adult Dose*</th>
<th>Pediatric Dose*</th>
<th>Frequency of Dosing*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cyclizine</td>
<td>50 mg IM</td>
<td>1 mg/kg/IM (maximum 25 mg)</td>
<td>q4-6h</td>
</tr>
<tr>
<td>Diphenhydramine</td>
<td>10-50 mg I.V.</td>
<td>1 mg/kg/ I.V.</td>
<td>q6-8h</td>
</tr>
<tr>
<td>Dolasetron</td>
<td>12.5 mg I.V. or 100 mg PO</td>
<td>0.35 mg/kg I.V. (maximum 12.5 mg)</td>
<td>single dose</td>
</tr>
<tr>
<td>Droperidol</td>
<td>0.625-1.25 mg I.V.</td>
<td>25-75 mcg/kg I.V.</td>
<td>single dose</td>
</tr>
<tr>
<td>Granisetron</td>
<td>0.1-1.0 mg I.V.</td>
<td>40 mcg/kg I.V.</td>
<td>single dose</td>
</tr>
<tr>
<td>Hydroxyzine</td>
<td>25-100 mg IM</td>
<td>1 mg/kg/ I.V.; IM</td>
<td>q6h</td>
</tr>
<tr>
<td>Metoclopramide</td>
<td>10-20 mg I.V.</td>
<td>0.1-0.25 mg/kg I.V.</td>
<td>q6h</td>
</tr>
<tr>
<td>Ondansetron</td>
<td>1-4 mg I.V.</td>
<td>0.05-0.1 mg/kg I.V. (maximum 4 mg)</td>
<td>single dose</td>
</tr>
<tr>
<td>Prochlorperazine</td>
<td>5-10 mg I.V.</td>
<td>0.1 mg/kg PR</td>
<td>q12h</td>
</tr>
<tr>
<td>Promethazine</td>
<td>12.5-25 mg I.V.</td>
<td>0.25-1 mg/kg PR</td>
<td>single dose</td>
</tr>
<tr>
<td>Scopolamine</td>
<td>0.3-4.65 mg I.V., IM</td>
<td>6 mcg/kg I.V., IM, SC</td>
<td>q4-6h</td>
</tr>
<tr>
<td>Trimethobenzamide</td>
<td>300 mg PO, I.V.</td>
<td>200 mg PR</td>
<td>100 mg PR, PO if &lt;15 kg 200 mg PR, PO if &gt;15 kg</td>
</tr>
</tbody>
</table>

*According to package inserts.

IM, intramuscular; I.V., intravenous; PO, per os; PR, per rectum; SC, subcutaneous

Table 5. Anesthetic Strategies To Reduce Incidence of PONV in Patients at Risk

- Premedicate the patient as needed to reduce anxiety.
- Prehydrate the patient to avoid hypotension.
- Avoid the use of nitrous oxide and potent inhaled agents when possible.
- Choose regional anesthetic techniques when possible.
- Use propofol for the induction and maintenance of anesthesia.
- Use agents that reduce the need for opioids.
- Administer combination antiemetics prophylactically and intraoperatively.

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effects is lower. Excessive postoperative sedation, common when patients are given higher doses of droperidol, has in the past limited its use in outpatient anesthesia, but 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 requirement by the US Food and Drug Administration for a “black box” warning on droperidol labeling has reduced its role from that of an effective and safe prophylactic agent to that of a rescue agent for intractable cases of PONV. The concern is about the development of a prolonged QTc interval in some patients who receive droperidol, putting them at risk for torsades de pointes, a ventricular arrhythmia. Despite limited evidence that antiemetic doses trigger this arrhythmia, the “black box” warning requiring electrocardiographic monitoring remains part of the droperidol package insert.

The antihistamines diphenhydramine, hydroxyzine, and cyclizine prevent nausea and vomiting by acting on histamine H1 receptors. Their use as postoperative agents is limited by a high rate of sedation and dry mouth. Other troubling side effects include dysphoria, confusion, disorientation, visual disturbances, and hallucinations. Some studies have suggested that the efficacy of scopolamine in the prevention of PONV is no greater than that of placebo. Recently, however, scopolamine in the form of a transdermal patch applied the evening before or the morning of surgery has been shown to reduce PONV as effectively as ondansetron. The study by Tang and colleagues reported effective prophylaxis of PONV in a high-risk patient population when the transdermal scopolamine patch was applied on the morning of surgery. The reduced incidence of PONV was achieved with insignificant side effects (e.g., dry mouth) and at only 25% of the cost of I.V. ondansetron at their institution.

Metoclopramide and trimethobenzamide are benzamide compounds that act on central dopamine and serotonin receptors, with both prokinetic and antiemetic effects. Metoclopramide, which increases gastrointestinal tract motility and thus decreases gastric volume and emptying time, is usually well tolerated by adult patients. The side effects of this class of agents, which include extrapyramidal effects and dystonia, are more often seen in the pediatric population. Unlike the agents discussed previously, metoclopramide is not associated with sedation, which makes it more attractive for outpatient treatment or prophylaxis. However, some studies have suggested that metoclopramide is considerably less effective than other agents, whether sedating or not, in the treatment of established PONV.

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. 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 an earlier study by Tang and colleagues, preoperative ondansetron was shown to be as useful as droperidol in the prevention and treatment of PONV, although less cost-effective considering that the administration of droperidol was not associated with an increased length of stay or other adverse side effects. Quinidine 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 those receptors known to be involved in emetogenesis may be effective in reducing PONV indirectly by mitigating symptoms known to be emetogenic. Agents such as midazolam or dexamethasone, for example, may reduce the nausea and vomiting that commonly accompany anxiety. As discussed previously, agents that reduce the need for opioids can be used prophylactically in patients at risk for PONV. Ephedrine and other agents used to maintain blood pressure may help prevent the nausea associated with hypotension.

The prophylactic use of single doses of steroids for PONV has become commonplace at many institutions. Dexamethasone, previously used in combination therapy, has been shown to reduce the incidence of PONV when administered alone and is now frequently given as a sole agent. Several studies have examined the efficacy of dexamethasone 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 in the study who received dexamethasone reported no more adverse events than those who received a placebo. In addition, the patients in the dexamethasone group in whom PONV developed were significantly less likely to require rescue antemetics. When used as the sole antiemetic agent for women undergoing laparoscopic gynecologic surgery, dexamethasone was shown to significantly reduce the incidence of PONV. The study authors, Laiq et al, concluded that dexamethasone—given its availability, low cost, and few side effects—should be given more frequently as a prophylactic antiemetic in women undergoing gynecologic laparoscopic surgery.

Because pharmacologic interventions have been unable to eliminate PONV, investigators have looked into the potential benefits of nonpharmacologic interventions. In a randomized, prospective, double-blind, placebo-controlled study by Agarwal and colleagues, the KD2 point (Korean hand acupuncture point in Koruy Hand Therapy) was evaluated for efficacy in the prevention of PONV. The placement of capsaicin ointment on the K-D2 point of each hand 1 hour before laparoscopic cholecystectomy resulted in a significantly lower incidence of PONV. The need for rescue antiemetic treatment was also lower. Stimulation of the P6 acupressure point has been associated with decreased PONV in high-risk women. This technique has been shown to increase patient tolerance to experimental nauseogenic stimuli and to reduce the number of symptoms.

A combination of antiemetic agents has been shown to reduce the incidence of PONV in patients at risk to a level significantly lower than that achieved with any agent alone. Combination therapy is most cost-effective for patients at high risk for PONV; medium-risk patients are often successfully treated with a single agent. Table 5 summarizes anesthetic strategies for patients at risk.

It is interesting to note that in one survey, the patients were willing to pay $100 out of pocket to prevent PONV, and 76% believed that avoiding PONV was important. The single incidence of postoperative vomiting has been calculated to exceed $300. Although dexamethasone and droperidol are the least expensive of the antiemetics, single doses of the serotonin antagonists generally cost less than $20.

Management of the Case

Our patient presented with factors that put her at risk for PONV. She was a menstruating woman, but most importantly, she had a history of intractable PONV and was a nonsmoker. In addition, she was scheduled to undergo a procedure known to increase her risk for PONV. Given her history, the decision was made to proceed with a spinal technique, thus avoiding those general anesthetic agents known to increase the incidence of PONV. The patient was premedicated with 2 mg of midazolam and 10 mg of metamizol. One liter of fluid was administered before placement of the neuraxial block. The patient received 10 mg of dexamethasone and 4 mg of ondansetron immediately after administration of the regional anesthetic had been completed.

The patient’s blood pressure was checked every 2 minutes to recognize and treat hypotension quickly. The intraoperative course was uncomplicated, and the patient was discharged home following 1.5 hours in the postanesthesia care unit. At follow-up (24 hours after discharge), she reported no symptoms of PONV. Although a clinician should never promise a patient an emesis-free experience, in this case we were able to prevent a repetition of the patient’s previously unpleasant experience with anesthesia.

Conclusion

The anesthesiologist is charged with both the prevention and the treatment of PONV. Although PONV develops in fully one third of patients, this generally manifests in the form of 1 or 2 episodes of emesis associated with nausea; the incidence of intractable PONV is <1%. PONV prophylaxis in low-risk patients is neither cost-effective nor indicated. Most medium- to high-risk patients can be treated effectively with a single agent. The plan for administering anesthesia to a patient at high risk for PONV should include premedication to reduce anxiety, the use of 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 should be used for induction and maintenance to avoid or reduce the need for N2O and the potent inhaled agents. A combination of antiemetic prophylactic agents should be administered to those judged to be at high risk for PONV, and adequate IV therapy should prevent the development of dehydration and hypotension postoperatively.

References

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Lesson 251: PreAnesthetic Assessment of the Patient With a History of Prolonged Postoperative Nausea and Vomiting

Post-test

1. The overall incidence of PONV is currently estimated to be:
   a. practically 100%
   b. 17%
   c. 30%
   d. entirely dependent on the duration of surgery

2. A factor that increases the risk for PONV is:
   a. a history of smoking
   b. male gender
   c. 30%
   d. entirely dependent on the duration of surgery

3. Patients who should routinely receive antiemetic prophylaxis include:
   a. those with a history of PONV
   b. all female smokers
   c. candidates for abdominal surgery
   d. those receiving general inhalation anesthesia

4. The anesthetic technique associated with the lowest incidence of PONV is:
   a. an inhalation technique that avoids N2O
   b. a balanced anesthetic technique
   c. an N2O- and opioid-based technique
   d. total I.V. anesthesia with propofol

5. Side effects of commonly used antiemetic agents include all of the following except:
   a. sedation
   b. agitation
   c. malignant hypothermia
   d. hallucinations

6. The risk for PONV can be reduced by:
   a. withholding I.V. fluids preoperatively
   b. administering ketorolac to control postoperative pain
   c. encouraging the patient to move as soon as possible postoperatively
   d. using patient-controlled analgesia with morphine to manage postoperative pain

7. The factor that most limits the route of use of serotonin antagonists in low-risk patients is:
   a. cost-effectiveness profile
   b. association with postoperative sedation
   c. risk for cardiac arrhythmias
   d. poor efficacy profile

8. Which of the following statements about droperidol is false?
   a. It is a very cost-effective agent.
   b. It acts on central dopaminergic receptors.
   c. Its side effects include sedation, lethargy, and agitation.
   d. It is associated with a high incidence of torsades de points.

9. Each of the following agents is a phenothiazine compound except:
   a. promethazine
   b. prochlorperazine
   c. hydroxyzine
   d. chlorpromazine

10. Of the following agents used in the treatment of PONV, the lowest incidence of postoperative sedation is associated with:
    a. promethazine
    b. droperidol
    c. scopolamine
    d. granisetron

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