Post-operative nausea and vomiting

Post-operative nausea and vomiting (PONV) is a common complication of surgery and anaesthesia. Although it is rarely fatal, PONV is unpleasant and associated with patient discomfort and dissatisfaction with their peri-operative care. Patients have reported that avoidance of PONV is of greater concern than avoiding post-operative pain. PONV is also associated with delayed discharge from the recovery room and prolonged hospital care and, therefore, increases health care costs.

Morbidity associated with PONV includes wound dehiscence, dehydration, electrolyte disturbance, interference with nutrition and, more rarely, oesophageal rupture (Boerhaave syndrome) or aspiration pneumonitis.

It is important that staff involved in caring for surgical patients understand PONV. A questionnaire-based study in 2000 demonstrated knowledge gaps, with only 60 per cent of ward nurses questioned giving correct responses.1

Physiology

Nausea is the sensation associated with the awareness of the urge to vomit. Vomiting is the forceful expulsion of upper gastrointestinal contents via the mouth, brought about by powerful sustained contraction of the abdominal muscles. Both are protective reflexes against the absorption of toxins (which trigger chemoreceptors in the gastrointestinal tract) but can also occur in response to olfactory, visual, vestibular and psychogenic stimuli.

Nausea is not well understood. It is associated with gastrointestinal relaxation, retroperistalsis in the duodenum, increased salivation, pallor and tachycardia. Vomiting and retching (repeated attempts to vomit without stomach contents being expelled) are brainstem responses; nausea involves higher brain regions.

Vomiting begins with deep breaths, closure of the glottis and elevation of the soft palate. The diaphragm then contracts strongly and the abdominal muscles contract to raise the intra-gastric pressure. This causes forceful ejection of gastric contents up the oesophagus and out of the mouth.

The exact nature of vomiting pathways are also not fully understood but a number of pathophysiological mechanisms known to cause nausea or vomiting have been identified.

In one study, these factors were shown to be additive. The risk of PONV in the presence of no, one, two, three and all four risk factors was 10, 20, 40, 60 and 80 per cent, respectively.

Females have a higher incidence of PONV than males and those of reproductive age suffer up to three times more often with PONV than men. This suggests a hormonal influence. Patients who have a history of motion sickness or previous PONV can have a well developed reflex arc for vomiting so are at an increased risk of PONV.

Opioids contribute to PONV via stimulation of the CTZ.

Other patient-specific factors

Age is thought to play a role in risk of PONV and emesis occurs less frequently in elderly patients. Post-operative pain and the analgesia given to manage it, movement and ambulation, eating too early after surgery, hypotension and hypoxaemia can all contribute to PONV. Risk factors also include obesity and gastric stasis.

Obesity

Studies have suggested an increased risk of PONV in obese patients, possibly
because of the longer time required to clear fat-soluble anaesthetic agents. Obese patients also have higher residual gastric volumes and an increased incidence of oesophageal reflux.

Delayed gastric emptying Delayed gastric emptying is also associated with increased incidence of vomiting. This delay can be due to pain, anxiety, disease process (e.g. gastric outlet obstruction) or the administration of opioids. Pre-operative anxiety raises levels of endogenous catecholamines, which stimulate CTZ receptors. Anxious patients can also swallow air causing gastric distention, which contributes to PONV.

Surgical factors The type of surgery influences the incidence of PONV. Intra-abdominal surgery, ophthalmic surgery (particularly for strabismus), gynaecological surgery and middle ear surgery are all associated with higher rates of PONV. The high incidence of PONV following open abdominal or intra-abdominal laparoscopic surgery may be due to gut ischaemia releasing 5HT.

It has been suggested that the longer the surgery the greater the incidence of PONV, possibly due to post-operative ileus (associated with extensive bowel handling during surgery and bowel wall oedema in longer procedures). Adequate but not excessive hydration has been reported to reduce the incidence of PONV.

Orthopaedic surgery has a lower risk of PONV because there is less autonomic stimulation than during abdominal surgery and patients are more likely to receive a regional anaesthetic.

Anaesthesia The anaesthetic induction agent etomidate is associated with an increase in PONV compared with thiopental sodium or propofol. Propofol (for induction or maintenance of anaesthesia as part of a total intravenous anaesthetic technique [TIVA]) has been reported to reduce the risk of PONV.

Of the volatile inhaled anaesthetic agents, sevoflurane and desflurane are reported to be associated with lower rates of PONV than enflurane or halothane. Nitrous oxide increases the incidence of PONV. It affects central opioid receptors, causes changes in middle ear pressure and causes bowel distention.

The use of intubation is thought to increase risk of PONV because of pharyngeal mecanochoreceptor afferent stimulation. Peripheral nerve blocks, total intravenous anaesthetic techniques and regional anaesthesia are all associated with a lower incidence of PONV than general anaesthesia with intubation and a traditional volatile agent dependent anaesthetic technique (see Resources).

Gastric inflation during mask ventilation can cause PONV because gaseous distention of the stomach and upper small intestine activates mechanoreceptors, sending afferent signals via the vagus nerve. If nitrous oxide is used, subsequent diffusion of the gas into spaces in the intestine worsens this situation. Avoidance of nitrous oxide during any anaesthetic can decrease the incidence of PONV, particularly in patients undergoing abdominal surgery.

It has been suggested that patients cared for by experienced anaesthetists have a lower incidence of PONV than those cared for by inexperienced anaesthetists. Possible explanations include that inexperienced anaesthetists accidentally insufflate more gas into the stomach or do not give prophylactic antiemetics.

Drugs Many drugs given peri-operatively affect the incidence of PONV. For example, premedication with atropine or opioids (e.g., morphine for analgesia) delays gastric emptying. Atropine also lowers oesophageal tone. Neostigmine, used to reverse residual muscle relaxation at the end of surgery, also increases the risk of PONV. Other common peri-operative drugs that can contribute to PONV include:

- Those with actions on the CTZ (e.g. opioids, dopamine, cytotoxic chemotherapeutic drugs)
- Those causing gastrointestinal irritation (e.g. non-steroidal anti-inflammatory drugs, iron supplements)
- Those causing gastric stasis (e.g. opioids, hyoscine butylbromide)

Management of PONV It is often easier to treat nausea and prevent vomiting than to stop vomiting once it has started. Identifying levels of risk helps staff to select appropriate action. Patients identified as low-risk do not usually need prophylaxis, unless there is risk of serious morbidity if vomiting does occur. Those at moderate or high risk of PONV will benefit from prophylaxis with an agent that prevents nausea and an appropriate anaesthetic technique. In some circumstances, such as where a patient has his or her jaws wired (e.g. following maxillofacial surgery) or has raised intracranial pressure, every effort must be made to avoid PONV.

Prophylaxis should include identification of risk factors for PONV, reducing them where possible and administering appropriate anti-emetic drug(s) at appropriate dose intervals. For example, opioids are highly emetogenic — they directly activate the CTZ, slow gastrointestinal motility and stimulate the vestibular nerve. Risk can, therefore, be reduced by substituting a non-opioid analgesic where appropriate. If opioids are necessary, the lowest possible doses should be used. Fentanyl and alfentanil are less likely to cause PONV than morphine and pethidine but have a short duration of action.

The choice of prophylactic agent should be based on level of risk, efficacy of agents available, their side effect profiles and the cost of prophylaxis versus the cost of treating vomiting. Patients at moderate risk should be considered for monotherapy, whereas high-risk patients can require several prophylactic agents with different pharmacological actions.

There are four main classes of drugs used in the management of PONV: anticholinergics, antihistamines, D₂ antagonists and 5HT₃ antagonists. However, because of the many ways in which the vomiting centre can be

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have weak muscarinic (vomiting centre and vestibular centre) and histamine receptor blocking activity. They act against agents that directly stimulate the CTZ (e.g., opioids, cytoxics and general anaesthetics) and are active against emetic stimuli arising from the gastrointestinal tract.

Antiparkinsonian side-effects include akathisia, dystonia and dyskinesia. Prochlorperazine is probably the commonest phenothiazine used for PONV. It is available as oral, buccal, rectal and parenteral preparations.

**Butyrophonenes** Butyrophenones (e.g., haloperidol) block D2 receptors in the CTZ. They have similar properties to phenothiazines but are not commonly used for PONV. Droperidol was withdrawn in 2001, following a risk-benefit assessment because of concerns about its potential effect on prolonging the cardiac QT interval.

5HT3 antagonists 5HT3 receptor antagonists (e.g., ondansetron, dolasetron, tropisetron and granisetron) have proven efficacy in nausea and vomiting, and limited side effects. They specifically block 5HT3 receptors, both peripherally in the gut (5HT3 receptors of the vagal afferent nerves) and centrally in the CTZ. This action subsequently decreasesafferent visceral and CTZ stimulation of the vomiting centre respectively.

**Other agents** Dexemethasone is the steroid most commonly used for PONV. It is almost always used in combination with other agents. Its mechanism of action is unclear, but could be due to inhibition of prostaglandin formation. Adverse effects are not likely following a single bolus dose.

Somatostatin analogues (e.g., octreotide) have been used to reduce vomiting as a consequence of surgery. It reduces gastrointestinal secretions and motility.

Synthetic derivatives of cannabis (e.g., nabilone) have been found to have antiemetic properties and are useful in preventing vomiting caused by CTZ stimulation. Their effect is antagonised by naloxone. Neurokinin-1 receptor antagonists (e.g., aprepitant) selectively antagonise substance P at human neurokinin-1 receptors. Both nabilone and aprepitant are currently only licensed for use in nausea and vomiting caused by cytotoxic chemotherapy.

**Single versus multiple drug use** Generally, the use of a single anti-emetic reduces the incidence of PONV by about 30 per cent. Combinations of anti-emetics acting on different receptors are superior to monotherapy and drugs with different mechanisms of action should be used where a single agent has not been effective. It is beyond the scope of this article to look at the efficacies of different combinations studied.

**Treatment** If patients do vomit treatment should be given. Rescue therapy is usually administered parenterally, rectally or via buccal mucosal absorption. If PONV continues over a long period, anti-emetics can be given by continuous infusion using a syringe driver intravenously or subcutaneously. Physical and chemical stability of drugs needs to be considered if the anti-emetics are to be added to an infusion containing another drug (e.g., syringes containing an analgesic).

**Alternative treatments** Acupuncture at the Chinese acupuncture point P6 has been shown in many studies to decrease the incidence of nausea, including post-operative nausea. The acupuncture is usually applied before the procedure and can be continued for several days post-operatively. There are no side effects with this treatment.

Ginger and peppermint have also been used for many centuries to relieve nausea. Ginger is useful for post-operative nausea, once the patient has started to eat again. Peppermint is more commonly given as an infusion to drink. It is thought to act as a muscle relaxant in the gastrointestinal tract. Note that interactions can occur between large doses of peppermint and statins or feldopidine.

**References**

**Resources**
- The Royal College of Anaesthetists provides patient resources, such as “What is anaesthesia?” Available at www.rcoa.ac.uk (accessed 22 November 2004).

**Action: practice points**
Reading is only one way to undertake CPD and the Society will expect to see various approaches in a pharmacist’s CPD portfolio.
1. Make sure your hospital has a policy for PONV
2. Try to find out the rationale for the different agents used in your hospital for managing PONV
3. Look at the evidence comparing different anti-emetic agents both singly and in multiple combinations for a range of surgical procedures.

**Evaluate**
For your work to be presented as CPD, you need to evaluate your reading and any other activities. Answer the following questions:
- What have you learnt?
- How has it added value to your practice? (Have you applied this learning or had any feedback?)
- What will you do now and how will this be achieved?