Nausea and vomiting

Christopher O’Brien MD CCFP FCFP

Gregg, a 64-year-old man, has a 40-pack-year smoking history. He presents with a 2-month history of cough and a recent episode of hemoptysis. A chest x-ray film reveals a right lung mass, and computed tomography (CT) of the chest, abdomen, and pelvis confirms a right middle lobe mass with no evidence of metastatic disease. Lung biopsy confirms non–small cell lung cancer (NSCLC) and results of further metastatic workup are negative. The tumour is stage IB (T2N0) NSCLC. After Gregg and his doctor discuss options, Gregg is referred to an oncologist and a chest surgeon. He elects to have a lobectomy and postoperative chemotherapy. Six weeks after the surgery, he is doing well and chemotherapy will commence shortly.

The oncologist informs Gregg of the potential side effects of chemotherapy, including nausea and vomiting.

Chemotherapy-induced nausea and vomiting (CINV) is triggered by stimulation of the chemoreceptor trigger zone (CTZ), which is located in the area postrema in the floor of the 4th ventricle of the brain (Figure 1).* It is sensitive to chemical stimulation from cerebral spinal fluid and blood. The dominant receptors in this area are serotonin type 3 (5-HT₃) and dopamine type 2 (D₂).¹-³

There are 3 types of CINV⁴:

• acute emesis, which occurs within 1 to 2 hours of chemotherapy,
• delayed emesis, which occurs 24 hours or more after chemotherapy, and
• anticipatory nausea and vomiting.

Gregg knows he will cope with hair loss and fatigue, but is anxious about the potential nausea and vomiting everyone talks about. He receives counsel on prophylaxis of CINV.

Prophylaxis of CINV

Serotonin receptor antagonists are highly effective in preventing CINV. They should be given on a schedule for prophylaxis. The following 5-HT₃ antagonists and schedules are available:

• 8 mg of ondansetron by mouth or intravenously every 8 or 12 hours;
• 1 to 2 mg of granisetron by mouth or intravenously once daily; or
• 5 mg of tropisetron by mouth or intravenously daily.

It is important to note that dexamethasone can augment the effects of 5-HT₃ antagonists and other antiemetics.

As chemotherapy is initiated, Gregg uses 8 mg of ondansetron twice daily for prophylaxis of nausea and vomiting. He does well, with only occasional breakthrough nausea, for which he uses diphenhydramine as needed. Diphenhydramine, however, is unsuccessful in treating the nausea. Why isn’t it effective, and what can be done?

Diphenhydramine in CINV

Diphenhydramine is not the best choice for CINV. It has both antihistamine and anticholinergic activity at the level of the vomiting centre, and it is most effective for treating motion sickness. The pathophysiology behind Gregg’s nausea suggests a better choice would be a medication with both dopamine D₂ antagonist and serotonin type 4 (5-HT₄) agonist qualities,³ such as 10 mg of metoclopramide 4 times daily or as needed.

Ten mg of metoclopramide 4 times daily as needed is added to Gregg’s scheduled ondansetron. He achieves complete relief of his nausea and vomiting. Starting his fourth round of chemotherapy, Gregg forgets to premedicate with ondansetron and he experiences severe nausea and vomiting. Just before his fifth round, he becomes very anxious and nauseated. What is the likely pathophysiology of the nausea and vomiting, and how can it be treated?

Anticipatory nausea and vomiting

Anticipatory nausea and vomiting before chemotherapy is often associated with a memory of poorly controlled nausea and vomiting.⁴ It is a function of higher brain centres (the cerebral cortex), where meaning and emotion interface with the vomiting centre. This mechanism is best managed with a preventive approach, using anxiolysics (eg, lorazepam) hours to days before expected chemotherapy.

Gregg completes his chemotherapy and follows up with the oncologist every 3 months. He feels well and is not using any medication. Eight months later, he presents with a 6-week history of fatigue and anorexia, and a 2-week history of right-sided chest and midback pain. He describes the pain as an ache—a score of 7 on a 10-point visual analogue scale. He has been using 2 Tylenol No. 3 tablets (left over from his surgery) 4 times daily, on average, along with ibuprofen, and is not getting much relief.

*Figure 1 is available at www.cfp.ca. Go to the full text of this article on-line, then click on CFPlus in the menu at the top right-hand side of the page.
While investigations are arranged, treatment is immediately initiated with a stronger opioid (hydromorphone) and naproxen sodium. A chest x-ray film reveals bilateral lung masses, and a subsequent CT and bone scan show a recurrence of a lung tumour with bone metastases to ribs and thoracic spine. Potential radiotherapy is discussed with the oncologist.

Within a week, hydromorphone is titrated to 3 mg every 4 hours, on schedule, and pain relief is achieved—a score of 2 on a 10-point scale. Gregg now reports frequent nausea, and vomits daily. What are the potential causes of Gregg’s nausea and vomiting, and how should it be managed?

More causes
There are several other causes of nausea and vomiting in palliative care:

Drug induced
Opioid induced: High plasma concentrations of emetogenic substances (opioids, selective serotonin reuptake inhibitors, urea, and calcium) trigger nausea and vomiting by stimulating dopamine D₁ receptors located in the CTZ. The best treatment would be a dopamine antagonist, such as haloperidol, which is the most potent of dopamine receptor blockers,⁴ and metoclopramide. Because metoclopramide has a dopamine D₂ antagonist effect, muscarinic activity, and is a 5-HT₄ receptor agonist,⁵ it stimulates peristalsis in the upper gut and aids in impaired gastric emptying secondary to opioids.

Nonsteroidal anti-inflammatory drugs: Nonsteroidal anti-inflammatory drugs can result in gastritis or ulceration, causing nausea and vomiting. They should be either discontinued or a cytoprotective drug, such as a proton pump inhibitor, should be started.

Constipation. Constipation is common with opioids and often overlooked as a cause of nausea and vomiting. Treating constipation requires a preventive approach; a scheduled opioid demands a scheduled bowel regimen with few exceptions.

Hypercalcemia. Hypercalcemia should be anticipated in patients with bone metastases. It is a paraneoplastic syndrome associated with NSCLC. Hypercalcemia can be corrected with saline, diuretics, and bisphosphonates; nausea should be treated while waiting for effects. Hypercalcemia affects the CTZ, so the above-mentioned approach should be used.

Gregg uses 1 mg of haloperidol by mouth every 12 hours and 0.5 mg of haloperidol every 6 hours as required, for what is expected to be opioid-induced nausea and vomiting; the nausea improves. Within days, his nausea flares up and history reveals 6 days with no bowel movements. On digital rectal examination, a lot of hard stool is found in his rectum. Laboratory test results show normal calcium and blood urea nitrogen. The constipation is treated with a bisacodyl suppository and an enema, and a bowel maintenance regimen is followed.

Once his nausea and vomiting is stable, Gregg is advised about the natural history of opioid-induced nausea and vomiting and its self-limiting quality. His scheduled haloperidol use is stopped, but he continues to use the 0.5-mg dose of haloperidol as required. Gregg is aware that opioid-induced constipation is not self-limiting but here for the duration; therefore, he must continue the scheduled bowel regimen. He finishes his radiotherapy for bone and lung metastases, and his opioid dose is eventually lowered.

The doctor addresses the palliative prognosis with Gregg and his family, and connects him with a local palliative home care team. A month later, Gregg’s condition deteriorates. The community nurse calls the doctor to inform him that Gregg is suffering from headaches, cognitive impairment, and nausea and vomiting. Brain metastases are suspected and are confirmed on CT. Gregg uses 8 mg of dexamethasone twice daily and his symptoms improve; the dexamethasone dosage is titrated to 4 mg twice daily. Gregg and his family discuss goals of care with the doctor; however, Gregg declines palliative radiotherapy for brain metastases. He is tired and only wants comfort measures. He is cared for at home and his symptoms are well managed until his death 7 weeks later.

Nonpharmacologic management of nausea and vomiting

Advise patients to do the following:

• Wear loose-fitting clothing.
• Eat small frequent meals. (If any of your patients prefer not to eat or drink in order to manage nausea and vomiting, recognize and respect their decision.)
• Avoid certain foods (sweet, fatty, high salt, or spicy food, or food with unpleasant odours).
• Maintain a relaxed atmosphere.
• Consult a dietitian to assess proper food portions and texture.
• Try complementary therapies (eg, diversion, relaxation, hypnosis, guided imagery, acupuncture).

Nonpharmacologic management of nausea and vomiting
Dr O’Brien is the Medical Director of the Palliative Care Program at Saint John Regional Hospital in New Brunswick.

Competing interests
None declared

References

Further reading


Points Saillants
- Les nausées et les vomissements, sources de maux fréquents et pénibles, nuisent à la qualité de vie des patients. Les nausées et les vomissements affectent jusqu’à 50 à 70% des patients qui souffrent d’un cancer évolué.
- Les déclencheurs des nausées et des vomissements peuvent souvent être expliqués grâce à un historique complet, un examen physique, une liste des médicaments actuels et un profil biochimique limité.
- En associant ces déclencheurs et nos connaissances de la pathophysiologie du mécanisme de vomissement et des récepteurs des neurotransmetteurs associés, on peut concevoir un régime antiémétique. Cela s’est montré efficace chez 93% des patients.
- Les patients à un stade avancé de maladie présentent souvent de multiples causes de nausées et de vomissements; il faut combiner une pharmacothérapie et des mesures générales pour les gérer. Chez quelques patients, il est possible d’identifier et de contrer les causes spécifiques des nausées et des vomissements.