Understanding nausea and vomiting in advanced cancer

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Nausea and vomiting are commonly experienced by people with advanced cancer. Nausea and vomiting can have an adverse effect on a patient’s physical, psychological and social well-being. Knowledge of the physiology of nausea and vomiting will promote a rational choice of treatment. Nurses also need to be aware of non-pharmacological measures that can reduce these distressing symptoms.

It is estimated that 20–60 per cent of patients with advanced cancer will experience nausea and vomiting (Allan, 1999; Grond et al, 1994; Dunlop, 1989; Baines, 1988). The patient with advanced cancer may have several potential causes for nausea and vomiting, although it is often possible to identify the primary cause. The primary cause, however, may change during the patient’s illness.

Nurses have a significant role in assessing symptoms, measuring the response to antiemetics and providing non-pharmacological treatments. Thorough assessment, knowledge of antiemetics and their mode of action, will allow the nurse to provide individualised treatment.

Nausea and vomiting can cause dehydration, electrolyte imbalance and nutritional deficiencies (Marek, 2003), and it can also impact on a patient’s psychosocial well-being. They may become withdrawn, isolated and unable to perform their usual activities of daily living. The patient’s distress often extends to family members.

Learning objectives

- Understand the physiology behind nausea and vomiting;
- Know the link between advanced cancer and nausea and vomiting;
- Be familiar with the assessment of nausea and vomiting;
- Know the different medications that can be used to treat nausea and vomiting;
- Understand the connection between nausea and vomiting and chemotherapy.

Definitions

Nausea and vomiting are often regarded as a single entity, but they are separate physiological conditions (Eckert, 2001). Nausea is an unpleasant feeling of the need to vomit. It is often accompanied by autonomic symptoms such as pallor, cold sweat, salivation and tachycardia (Yarbro et al, 1999). Retching is a strong involuntary effort to vomit. It occurs in the presence of nausea and often culminates in vomiting (Twycross and Back, 1998). Vomiting (emesis) is the forceful expulsion of gastric contents through the mouth (Twycross and Back, 1998).

After an episode of vomiting, there may be a post-ejection phase characterised by weakness, lethargy and shivering (Allan, 1999). Vomiting may ease the sensation of nausea. It may serve a protective function by expelling noxious substances from the gut and stop further ingestion of such substances (Allan, 1999; Yarbro et al, 1999).

Physiology

Synchronous contractions of the diaphragm and abdominal muscles raise intra-abdominal pressure and compress the stomach. Atony of the stomach, oesophageal sphincter and pylorus are associated with retroperistalsis. As a result, stomach contents are forced upwards to the mouth, culminating in the act of vomiting (Yarbro et al, 1999; Twycross and Back, 1998; Marieb, 1989).

Several neural structures and a variety of neurotransmitters and receptors have been identified that relate to nausea and vomiting. Most of the relevant receptors are excitatory – they induce nausea and vomiting when stimulated (Twycross and Back, 1998) (Fig 1).

The vomiting centre, sometimes referred to as a central pattern generator, is located within the reticular formation of the brain stem and is thought to coordinate the vomiting process. It lies completely within the blood-brain barrier and receives impulses from the chemoreceptor trigger zone (CTZ), vestibular apparatus (the part of the internal ear concerned with balance) higher cortical centres and afferent nerve impulses from the periphery (primarily via the vagus nerve, but also the glossopharyngeal nerve and sympathetic afferents). The vomiting process is coordinated by efferent impulses from the vomiting centre to the pharynx, larynx, diaphragm, intercostal muscles and gut.

The CTZ is located within the area postrema (on the floor of the fourth ventricle in the brain). Although anatomically close to the vomiting centre, the CTZ lies partly outside the blood-brain barrier and is therefore exposed to various noxious agents borne in the blood and cerebrospinal fluid – such as toxins, biochemical products and $\%$
Cancer care and Nausea

Keywords


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Pharmacology

Occasionally, assessment will reveal a specific cause of nausea and vomiting that is treatable (for example hypercalcaemia). However, antiemetic therapy is nearly always necessary for patients with advanced cancer. Many antiemetic drugs are available with varying modes of action, but none will provide complete control in all situations. The three most commonly used antiemetics in palliative care are metoclopramide, cyclizine and haloperidol (Back, 2001; Twycross and Back, 1998).

Metoclopramide affects the myenteric plexus through its action as a 5-HT4 agonist and D2 antagonist. Its proximal effect results in accelerated gastric emptying. At higher doses, metoclopramide antagonises D2 and 5-HT3 receptors in the CTZ (Yarbro et al, 1999; Baines, 1997).

Metoclopramide is the antiemetic of choice in cases of gastric stasis and partial gastric obstruction. It is also the first choice antiemetic in chronic, unexplained nausea (Twycross, 2004; Back, 2001).

Haloperidol is a more potent and more selective D2 antagonist than metoclopramide. It is used when there is thought to be a chemical cause for nausea and vomiting, such as secondary renal failure, hypercalcaemia or drug therapy (Twycross, 2004; Back, 2001).

Cyclizine acts on the vomiting centre and has antihistaminic and antimuscarinic properties. It is used when nausea is associated with complete bowel obstruction, vestibular disturbance and raised intracranial pressure.

Antimuscarinic drugs such as cyclizine should not be prescribed with a prokinetic such as metoclopramide as they have antagonistic properties.

If a single first-line antiemetic does not provide relief then health care professionals must question whether the cause has been correctly identified. Options include:

- Changing to an antiemetic that has a different action;
- Combining antiemetics with complementary action.

About one-third of patients with advanced cancer who experience nausea and vomiting require more than one antiemetic (Twycross, 1997). If first-line antiemetics fail to provide satisfactory relief, adding or substituting a second-line antiemetic such as levomepromazine or dexamethasone should be considered.

Levomepromazine is a phenothiazine with a broad spectrum of antiemetic properties. It has an antagonistic action on D2, H1, Ach m and 5-HT3 receptors (Twycross and Back, 1998; Baines, 1997). Dexamethasone also has antiemetic properties, although its mode of action is uncertain.

Referral to a specialist palliative care team is recommended for patients with advanced cancer whose symptoms are uncontrolled after 48 hours.

Route of administration

The three first-line antiemetics used in palliative care can be given orally and parenterally. Oral administration is the route of choice but may be a problem for those who:

- Are unable to swallow – due to dysphagia, frailty, unconsciousness;
- Are persistently vomiting;
- May not be absorbing the drug – this is uncommon except in cases of delayed gastric emptying, for example with nausea or obstructed gastric outflow;
- Are reluctant to take oral medication – for example because they are afraid of inducing vomiting.

When the oral route cannot be used, occasional episodes of nausea and vomiting may be relieved by injection. For persistent nausea and vomiting, a continuous subcutaneous infusion via syringe driver is the preferred method of administering an antiemetic (Baines, 1997). The syringe driver:

- Avoids the need for repeated injections;
- Produces relatively constant systemic levels of medication, avoiding medication peaks (increasing the risk of side-effects) and troughs (resulting in reduced symptom control);
- Has minimal impact on patient mobility;
- Allows medication to be administered over a 24-hour period (Perdue, 2004).

Chemotherapy

Nausea and vomiting are common side-effects of chemotherapy. Chemotherapy agents and radiation to the gut are thought to stimulate the enterochromaffin cells of the gastrointestinal tract, causing them to release 5-HT that binds to the 5-HT3 receptors located on the vagus nerve. The impulses are carried to the CTZ resulting in the sensation of nausea and the need to vomit (Marek, 2003; Yarbro et al, 1999).

Chemotherapy may damage the rapidly dividing cells of the gut leading to breaches in gut wall integrity. Such damage could allow emetogenic toxins to enter the bloodstream (Yarbro et al, 1999). Chemotherapy may also inhibit gastric emptying (Yarbro et al, 1999).

Several distinct types of nausea and vomiting have been associated with chemotherapy:

- Acute – occurring within the first 24 hours of treatment and related to the release of 5-HT from enterochromaffin cells;
- Delayed – occurring 24–72 hours after treatment. The causative mechanism is unclear but may be related to reduced gastric motility and gut wall damage;

Guided reflection

Use the following points to write a reflection for your PREP portfolio:

- Describe how this article is relevant to your work;
- Summarise the article’s main points about nausea and vomiting in advanced cancer;
- Identify new knowledge about nausea and vomiting you have learnt from this article;
- Consider how you will use this information in your future practice;
- State how you intend to follow up what you have learnt from this article.
**BOX 1. CAUSES OF NAUSEA AND VOMITING IN PATIENTS WITH ADVANCED CANCER**

- Drugs
  - Drugs cause nausea and vomiting in different ways:
    - Gastric irritation – NSAIDs non-steroidal anti-inflammatory drugs, iron supplements, antibiotics;
    - Gastric stasis – opioids, tricyclic antidepressants, anticholinergics;
    - 5-HT3 receptor stimulation – chemotherapy, selective serotonin re-uptake inhibitors (SSRIs);
    - Drugs with an unpleasant taste – docusate sodium (liquid), potassium supplements;
    - Excessive amounts of medication at any time.
    - Radiotherapy – especially on abdomen or head;
    - Gastric – gastric stasis, gastric obstruction (partial or complete), ‘squashed stomach syndrome’;
    - Constipation;
    - Metabolic – uraemia, hypercalcaemia;
    - Pain;
    - Pharyngeal stimulation – candida infection, tenacious sputum;
    - Psychosomatic factors – fear, anxiety, anticipatory nausea and vomiting, aversion to certain tastes, sights and odours;
    - Vestibular disturbance;
    - Ascites;
    - Concurrent causes – renal failure, peptic ulceration, alcohol gastritis, gastric infection.

*Sources: Twycross and Back, 1998; Baines, 1997; Twycross, 1997*

- Anticipatory – occurring within the 24 hours before treatment commences. Anticipatory vomiting is related to previously poorly tolerated chemotherapy and is less common since the introduction of effective antiemetic regimes. Trigger factors are often those associated with receiving the treatment, such as the journey to the chemotherapy unit, sights and smells or seeing the staff who administer the chemotherapy (Eckert, 2001).

- 5-HT3 antagonists, for example ondansetron and granisetron, are highly effective antiemetics used to treat acute nausea and vomiting induced by chemotherapy. A prokinetic such as metoclopramide has value in the treatment of delayed nausea and vomiting. Dexamethasone is used in the treatment of both acute and delayed nausea, although the mode of action remains unclear (Marek, 2003; Yarbro et al, 1999).

- There is no satisfactory treatment for anticipatory nausea and vomiting, and prevention is important. However, benzodiazepines may be tried. Non-pharmacological interventions have a particularly important role in anticipatory nausea.

Patients undergoing chemotherapy will experience nausea and vomiting to varying degrees. Factors that contribute to the severity of the symptoms include (Marek, 2003; Eckert, 2001):

- The chemotherapy agents used and their dosage;
- Age – it is more pronounced in younger people;
- Gender – females are more prone to chemotherapy-induced nausea and vomiting;
- Alcohol intake – a chronic, high alcohol intake reduces incidence of chemotherapy-induced nausea and vomiting;
- Individuals who suffer from motion sickness may experience more severe episodes of nausea and vomiting;
- Increased levels of anxiety.

**Non-pharmacological measures**

There is a range of non-pharmacological interventions that may help reduce the frequency and severity of symptoms, enhance the effect of antiemetics and increase the patient’s sense of control. Dietary measures may include:

- Eating foods cold or at room temperature as they often smell less strongly than hot foods;
- Avoiding fatty foods;
- Eating carbohydrates;
- Eating small, frequent meals;
- Avoiding foods that increase the patient’s nausea;
- Educating family members who, in their desire to ‘do the right thing’ encourage the patient to eat more than they can comfortably manage.

It can be argued that the patient’s favourite food should be avoided during episodes of nausea in case it provides a future stimulus for nausea and vomiting, so depriving the patient of a pleasurable experience.

Avoiding the sight and smell of food may reduce episodes of nausea. The inpatient should be protected from unpleasant odours, for example from bedside commodes, episodes of incontinence or malodorous wounds. Once the patient has finished eating, any remaining food should be quickly cleared away. Any used receptacles should be removed promptly after episodes of vomiting.

Occasionally, in cases of complete bowel obstruction where nausea and vomiting is intractable, the passing of a nasogastric tube or a venting gastrostomy may provide relief (Twycross, 2004). Abdominal paracentesis can ease symptoms when nausea and vomiting is associated with tense ascites.

Taking too many tablets at once can also induce nausea and vomiting in susceptible patients. When prescribing, medical staff should work closely with nursing colleagues to avoid burdening the patient with excessive numbers of tablets at any one time. Mouthwashes should be available after episodes of vomiting. The reassuring presence of a calm, competent and understanding nurse should not be underestimated.

Relaxation and positive imagery may prove beneficial in reducing the incidence of nausea and vomiting associated with anxiety. Acupuncture (Vickers, 1996) and acupressure (Dibble et al, 2000) can also be of benefit.