ABC of palliative care

Nausea, vomiting, and intestinal obstruction

Mary J Baines

Nausea and vomiting

Nausea, vomiting, and retching are common and distressing complaints: surveys have found that 50-60% of patients with advanced cancer suffer from one or more of these. These symptoms are more common in patients under 65 years old, in women, and in those with cancer of the stomach or breast.

Assessment

An understanding of the emetic process and the main neurotransmitters involved is helpful in assessing and treating patients who are vomiting because antiemetic drugs are predominately neurotransmitter blocking agents. They are effective at different receptor sites and therefore treat different causes of vomiting.

As well as the specific causes of vomiting resulting directly or indirectly from advanced malignancy, patients may develop unrelated conditions such as gastroenteritis or gall bladder disease. In most cases the cause of vomiting is multifactorial, but it is helpful in planning treatment to list all contributing factors.

The causes of vomiting can usually be determined from a careful history and clinical examination. Note should be taken of the volume, content, and timing of vomits. A biochemical profile may be needed, but other investigations are often inappropriate.

Management

Nausea can be treated with oral drugs, but alternative routes are needed for patients with severe vomiting. It must be remembered, however, that persistent nausea may decrease gastric emptying, with a resultant decrease in drug absorption. An antiemetic injection is suitable to control a single episode, but with a persistent problem it is preferable to give drugs by subcutaneous infusion using an infusion device such as a pocket sized syringe driver. Antiemetics, in suppository or tablet form, can also be given rectally, but buccal administration of antiemetics is poorly tolerated.

Non-drug methods are important; these include avoidance of food smells or unpleasant odours, diversion, and relaxation. Some patients report benefit from acupuncture or acupressure bands.

Specific cause of vomiting

In a few patients, a specific cause of vomiting can be identified and treated successfully. However, most patients have irreversible and multiple causes of vomiting and require treatment with antiemetics and other measures.

Opioid induced vomiting—About 30% of patients who receive morphine feel nauseated during the first week of treatment. Metoclopramide should be given prophylactically to cover this period. Haloperidol is an alternative.

Cytotoxic chemotherapy—The use of ondansetron, granisetron, or tropisetron—the 5-HT₃ receptor antagonists—has greatly improved the control of emesis, even with cisplatin. This effect is enhanced by combining the antiemetic with dexamethasone. High dose metoclopramide and dexamethasone is a less effective but cheaper alternative. Lorazepam is used to reduce anticipatory anxiety and nausea.

The emetic process—pathways of emesis and the neurotransmitters involved

Common causes of vomiting in patients with advanced cancer

• Drugs
Especially opioids and chemotherapy	• Biochemical causes
Renal failure
Hypercalcaemia
Infection
Tumour toxins
• Gastric causes
Gastritis or ulceration
Functional gastric stasis due to external pressure
Carcinoma of stomach
Gastroduodenal obstruction	• Raised intracranial pressure
• Vestibular disturbance
• Abdominal or pelvic radiotherapy
• Constipation
• Intestinal obstruction	• Anxiety
• Cough induced

Reversible causes of vomiting

Cause of vomiting	Treatment
Hypercalcaemia	Rehydration and bisphosphonates
Infection	Antibiotics
Raised intracranial pressure	Dexamethasone
Gastric irritation or ulceration	Stop non-steroidal anti-inflammatory drug Give omeprazole or H ₂ receptor antagonist
Constipation	Rectal measures and laxatives
Anxiety	Explanation and reassurance, possibly also anxiolytic drugs

Renal failure—Haloperidol is usually effective, although methotrimeprazine is sometimes required for intractable vomiting.

Functional gastric stasis—A prokinetic drug such as metoclopramide, domperidone, or cisapride should be used.

Inoperable gastroduodenal obstruction—Metoclopramide may be effective if the obstruction is partial. Dexamethasone was thought to shrink inflammatory oedema around an obstructive lesion, but it may work by reducing perineuronal oedema in a functional obstruction; its antiemetic effect may also be of benefit. Octreotide or high dose hyoscine butylbromide may reduce the volume of vomit, otherwise intubation will be required.

Raised intracranial pressure—If dexamethasone is contraindicated or ineffective, cyclizine is the antiemetic of choice.

Vestibular disturbance—Cyclizine is usually effective, but an alternative is sublingual or transdermal hyoscine hydrobromide.

Intestinal obstruction

Intestinal obstruction is caused by an occlusion to the lumen or a lack of normal propulsion that prevents or delays intestinal contents from passing along the gastrointestinal tract. Obstruction may cause the presenting symptoms of cancer, or may develop during the course of the disease. Any site in the bowel may be affected, from the gastroduodenal junction to the rectum and anus.

While surgery remains the primary treatment for malignant obstruction, it is now recognised that some patients with advanced disease or poor general condition are unfit for surgery and require alternative management to relieve distressing symptoms.

Aetiology

The overall incidence of intestinal obstruction in patients with advanced cancer is about 3%, but patients with advanced ovarian cancer have a risk of obstruction of 25-40%. Patients with metastatic abdominal or pelvic cancer often have both mechanical and functional causes for obstruction, which may occur at more than one site.

Assessment

Clinical features

The symptoms of intestinal obstruction will depend on the site of the problem, a high obstruction causing more severe vomiting. In patients with advanced disease the onset of obstruction is usually insidious, over some weeks. Symptoms may gradually worsen and become continuous, but even without treatment the symptoms may be intermittent and the obstructive episodes resolve spontaneously, if temporarily.

A distinction is often made between complete and partial obstruction, but this is far from easy in practice and, clinically, the obstruction may seem to alter from one type to the other on several occasions as the illness progresses.

Investigations

Radiological investigations are of value in only two clinical situations: firstly, to differentiate between constipation and malignant obstruction; and, secondly, to confirm the obstruction and determine its site and nature in a patient who is being considered for surgery.

Management

There are now several treatment options for patients with advanced cancer who develop intestinal obstruction. It is rarely

Recommended antiemetic drugs

Antiemetic	Dose (per 24 hours)*	Main site of action
<i>Prokinetics</i>		
Metoclopramide†	30-80 mg	Increase peristalsis in upper gut, also dopamine antagonists
Domperidone	30-80 mg	
Cisapride	20-30 mg	Increases peristalsis in gut
<i>Antihistamines</i>		
Cyclizine†	150 mg	Vestibular and vomiting centres
<i>Butyrophenones</i>		
Haloperidol†	1.5-10 mg	Blocks dopamine receptors at chemoreceptor trigger zone
<i>Phenothiazines</i>		
Methotrimeprazine†	12.5-75 mg	Blocks dopamine and serotonin receptors at chemoreceptor trigger zone, also acts at vestibular and vomiting centres
<i>5-HT₃ receptor antagonists</i>		
Ondansetron†	8-16 mg	Blocks 5-HT ₃ receptors at area postrema and in gut
<i>Corticosteroids</i>		
Dexamethasone†	8-20 mg	Reduces inflammatory oedema, also central and peripheral antiemetic effects
<i>Anticholinergics</i>		
Hyoscine butylbromide†	60-300 mg	Reduces gastrointestinal secretions and motility
<i>Somatostatin analogues</i>		
Octreotide†	300-600 µg	Reduces gastrointestinal secretions and motility

*A single dose will be about a third of this dose

†Can be given as subcutaneous infusion

Causes of intestinal obstruction in advanced cancer

- Extrinsic compression from enlargement of primary tumour, omental masses, malignant adhesions, post-irradiation fibrosis
- Intraluminal occlusion from annular tumour or polypoid lesions
- Motility disorders due to tumour infiltration of mesentery or bowel muscle (intestinal linitis plastica)

Radiograph showing intestinal obstruction

an emergency, so there is usually time to discuss the situation with patients and their family so that they can make an informed choice of the available treatments.

Palliative surgery

Palliative surgery should be considered for every patient with advanced cancer who develops intestinal obstruction. Some will have a non-malignant cause or an unrelated second primary tumour. However, mortality is high (12-30%), the mean survival time is short, and there is a high incidence of enterocutaneous fistulae.

Nasogastric intubation

This leads to a sustained relief of obstruction in only 0-2% of patients. It should therefore be used only for patients who are being considered for surgery and for those, principally with a high obstruction, who respond poorly to drug treatment. In this group, percutaneous venting gastrostomy should be considered as a better tolerated alternative. This can be performed under local anaesthesia.

Pharmacological treatment

Drugs have been used for years to relieve symptoms, and treatment regimens have gradually evolved. Continuous subcutaneous infusion is the preferred route of drug administration. This allows a combination of drugs to be given, and it is ideal for use in the home as it can be renewed every 24 hours by the visiting nurse.

The symptoms of colic, continuous abdominal pain, and vomiting usually occur together, and a typical starting prescription would be

- Diamorphine (dose depending on previous opioid dose)
- Hyoscine butylbromide 60 mg/24 hours
- Haloperidol 5 mg/24 hours.

If continuous pain or colic is not controlled, the dose of diamorphine or hyoscine butylbromide should be increased. If nausea and vomiting remain problems, cyclizine can be substituted for haloperidol or the two drugs can be used in combination. A useful alternative to this is methotrimeprazine, a highly effective antiemetic in this situation. However, if this fails, and especially if the total volume of vomits is large, octreotide is often used. It is antisecretory, proabsorbative, and reduces forward peristalsis. It can be combined with other drugs for subcutaneous infusion.

Corticosteroids have been widely used with apparent benefit to individual patients, but, with the intermittent nature of the early symptoms, it is difficult to know if the improvement is due to the corticosteroid treatment.

All patients will need regular mouth care. With good or moderate control of nausea and vomiting, patients can eat and drink as they choose, most favouring small and low residue meals.

A small group of patients, mainly with high obstruction, continue to vomit profusely in spite of medication. These may benefit from the insertion of a nasogastric tube or venting gastrostomy. The need for parenteral hydration should be decided on an individual basis; if indicated, fluids can be given by intravenous infusion or by hypodermoclysis (subcutaneous fluids). This is well tolerated and can be administered in the home supervised by the family and community nursing staff.

Symptoms of intestinal obstruction

- Nausea and vomiting
- Continuous abdominal pain
- Constipation
- Intestinal colic
- Distension
- Diarrhoea (with partial obstruction)

Treatment options in obstruction

- Palliative surgery
- Pharmacological treatment
- Nasogastric intubation
- Percutaneous venting gastrostomy

Factors associated with poor prognosis for palliative surgery

- Aged over 70 years, poor general medical condition or nutritional status
- Ascites, palpable abdominal masses, or distant metastases
- Previous radiotherapy to abdomen or pelvis
- Previous combination chemotherapy
- Multiple small bowel obstructions with radiographic evidence of prolonged transit time

Drugs used to relieve symptoms in intestinal obstruction

Drug	Dose (per 24 hours)	Comment
<i>Nausea and vomiting</i>		
Haloperidol	5-10 mg	Antiemetic of choice
Cyclizine	100-150 mg	May crystallise in infusion device
Methotrimeprazine	12.5-75 mg	Highly effective antiemetic Sedating at higher doses
Hyoscine butylbromide	60-300 mg	Reduces gastrointestinal secretions and motility
Octreotide	300-600 µg	Reduces gastrointestinal secretions and motility Expensive
<i>Intestinal colic</i>		
Diamorphine	As required	Usually an antispasmodic is also used
Hyoscine butylbromide	60-300 mg	Not sedating
<i>Continuous abdominal pain</i>		
Diamorphine	As required	
<i>Diarrhoea (from incomplete obstruction or faecal fistula)</i>		
Loperamide	6-16 mg (orally)	
Octreotide	300-600 µg	

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