Nausea and vomiting

Introduction

The management of nausea and vomiting for individuals receiving palliative care can be complex. As there may be several potential contributory factors to consider in any one individual, it may be useful to parallel the approach taken with pain management in palliative care and consider the concept of ‘total nausea’.

Assessment

- History – a separate history for both nausea and vomiting:
  - triggers, volume, pattern
  - exacerbating and relieving factors, including individual and combinations of drugs tried and routes used
  - bowel habit
  - medication – consider drugs that may:
    - contribute to the nausea and vomiting
    - cause harm
    - not take effect due to the nausea and vomiting
  - exclude regurgitation as this will require a different approach. If suspected consider seeking advice
  - check for other concurrent symptoms.

Examination:

- general review for signs of dehydration, sepsis and drug toxicity
- central nervous system
- abdomen (for example organomegaly, bowel sounds, succussion splash)
- check temperature, pulse and respiration

- Blood investigations where appropriate may include:
  - urea and electrolytes
  - liver function tests
  - calcium
  - blood glucose
  - therapeutic drug monitoring where indicated (for example digoxin, theophylline).

- Consider excluding urinary infection.

Clinical management - potential clinical scenarios

1. Clinical toxicity (including drug induced) or metabolic/biochemical upset (stimulation of chemoreceptor trigger zone [CTZ])

Clinical picture

- Persistent often severe nausea.
- Little relief from vomiting or retching.

Cause

- Chemical stimulation of CTZ.

By

- Drugs, including cytotoxics and opioids (also delay gastric emptying), NSAIDs, syrupy liquids, antibiotics, antidepressants, anticonvulsants, digoxin/cardiac drugs, alcohol.
- Metabolic, for example uraemia, hypercalcaemia, hyponatraemia, ketoacidosis, infection, Addison's disease, circulating toxins, hormone imbalance.
- Carcinomatosis/chronic inflammation (cytokine induced).

Treatment

- Treat metabolic imbalances.
- Dopamine antagonist, for example QT**metoclopramide**(caution in use of prolonged higher doses, monitor for extrapyramidal side effects) 10mg up to four times a day orally or subcutaneously or 30mg to 60mg over 24 hours by continuous subcutaneous infusion (unlicensed use). Specialists may recommend higher doses.

or

- QT† haloperidol 500micrograms to 1.5mg orally at night or twice daily, or 500micrograms to 1mg subcutaneously daily (start with lower doses in renal failure and elderly and frail patients) or 1mg to 5mg over 24 hours by continuous subcutaneous infusion titrated to effect (unlicensed use)
- QT† levomepromazine* 2.5mg to 5mg by subcutaneous injection 12 hourly as needed or 5mg to 15mg in 24 hours by continuous subcutaneous infusion. May need to give subcutaneous injection more frequently initially, for example hourly, to control symptoms. Consider change to oral route if symptoms resolve.
- Cytotoxic/systemic therapy induced – check local policy.

For persistent problems, seek specialist advice.

2. Motility disorders

Clinical picture

- Intermittent large volume vomit, usually relieves symptoms temporarily.
- Early satiation.
- Reflux, hiccup.
- Often little nausea until immediately prior to vomit.

Cause

- Gastric stasis.
- Gastric outlet obstruction - pseudo-obstruction - intestinal.

By

- Autonomic neuropathy (paraneoplastic).
- Drugs (opioid, anticholinergic).

- Metabolic (for example hypercalcaemia).
- Mechanical obstruction, tumour, nodes, enlarged liver (leading to squashed stomach).
- If there is large volume vomiting and/or colicky bowel pain, especially colic caused by a prokinetic agent - exclude complete bowel obstruction – refer to separate guideline.

Treatment - prokinetic

- QTMetoclopramide 10mg orally up to four times a day or 30mg to 60mg/24 hours by subcutaneous infusion (unlicensed route/dose/duration). Specialists may recommend higher doses.

or

- If elderly or at higher risk of extrapyramidal effects, use QTdomperidone 10mg three times a day orally (treatment lasting over one week will require closer monitoring due to cardiac risks).
- If extrinsic compression, consider stent insertion where appropriate or corticosteroid – †dexamethasone 4mg to 8mg daily reducing after 3 days, aiming to stop or reduce to lowest maintenance dose.

Note: prokinetic agents may trigger oesophageal spasm.

For persistent problems, seek specialist advice.

3. Intracranial disorders, for example raised intracranial pressure, vestibular dysfunction, movement-related nausea

Clinical picture

- Headache.
- Altered conscious level.
- Vertigo - dizziness with nausea.
- Movement-related sickness.

Cause

- Raised intracranial pressure (ICP), vestibular nerve or inner ear stimulation.

By

- Space occupying lesion.
- Base of skull tumour.
- Ototoxicity.
- Middle ear problems.

Treatment - raised intracranial pressure

- Cyclizine 25mg to 50mg orally or subcutaneously (unlicensed route) three times per day or 50mg to 150mg over 24 hours via subcutaneous infusion (unlicensed route).
- Corticosteroid – †dexamethasone 8mg to 16mg daily reducing after 3 days, aiming to stop or reduce to lowest maintenance dose.
- Second line – levomepromazine* QT 3mg to 6mg twice daily orally or QT †2.5mg to 5mg by subcutaneous injection 12 hourly as needed or 5mg to 15mg in 24 hours by continuous subcutaneous infusion. May need to give subcutaneous injection more frequently initially, for example hourly, to control symptoms

- QTprochlorperazine 3mg buccal or 5mg to 15mg orally.

Treatment - movement related nausea

- Cyclizine 25mg to 50mg orally or subcutaneously (unlicensed route) three times per day or 50mg to 150mg over 24 hours via subcutaneous infusion (unlicensed route)
- †Hyoscine hydrobromide 150micrograms to 300micrograms orally, 200micrograms to 400micrograms subcutaneously or 1mg/72 hours via transdermal patch. Observe for anticholinergic side effects.
- Cinnarizine 30mg orally initially then 15mg three times a day.
- Second line - levomepromazine* QT3mg to 6mg twice daily orally or QT†2.5mg to 5mg by subcutaneous injection 12 hourly as needed or 5mg to 15mg in 24 hours by continuous subcutaneous infusion. May need to give subcutaneous injection more frequently initially, for example hourly, to control symptoms
- QTprochlorperazine 3mg buccal or 5mg to 15mg orally.

For persistent problems, seek specialist advice.

4. Oral/pharyngeal/oesophageal irritation

Clinical picture

- Worse on eating.
- Exacerbated by sight or smell of food or smells from other sources.
- Reflux symptoms.
- Retching associated with productive cough.

Cause

- Cranial nerve irritation (vagal and glossopharyngeal).

By

- Tumour.
- Secretions or sputum, stimulating the gag reflex.
- Acid reflux.
- Toxins.
- Inflammation.
- Infection (for example candida, herpes simplex).
- Foreign body (for example stent).
- Smells from wounds, stomas, food or other sources.

Treatment

- Treat reversible causes, for example acid reflux, infection, secretions.
- Cyclizine 25mg to 50mg orally or subcutaneously (unlicensed route) three times per day or 50mg to 150mg over 24 hours via subcutaneous infusion (unlicensed route).
- Anticholinergics, for example † hyoscine hydrobromide 150micrograms to 300micrograms orally, 200micrograms to 400micrograms subcutaneously or 1mg/72 hours via transdermal patch.
- Levomepromazine* QT 3mg to 6mg twice daily orally or QT † 2.5mg to 5mg by subcutaneous injection 12 hourly as needed or 5mg to 15mg in 24 hours by continuous subcutaneous infusion. May need to give subcutaneous injection more frequently initially, for example hourly, to control symptoms.

For persistent problems, seek specialist advice.

5. Multifactorial/unknown/refractory

Clinical picture

Treatment

- Consider potential causes and treat appropriately. If nausea and vomiting persists, use levomepromazine* as a broad spectrum anti-emetic.
- levomepromazine* QT3mg to 6mg twice daily orally or QT†2.5mg to 5mg by subcutaneous injection 12 hourly as needed or 5mg to 15mg in 24 hours by continuous subcutaneous infusion. May need to give subcutaneous injection more frequently initially, for example hourly, to control symptoms maintenance dose.
- Consider higher centre origin, for example pain, fear, anxiety.

For persistent problems, seek specialist advice.

6. Higher centres (pain/fear/anxiety)

Treatment

- Refer to Pain assessment and Pain management guidelines where appropriate.
- Nausea associated with anticipation or anxiety may respond to a benzodiazepine, for example lorazepam 500 micrograms to 1mg sublingually or diazepam 2mg to 5mg orally or midazolam 2mg to 5mg subcutaneously or 5mg to 10mg over 24 hours in a syringe pump. The 500 microgram Lorazepam tablet cannot be absorbed by this route. Only the blue 1mg tablets, which can be halved, can be used (e.g. TEVA, Genus, PVL).

For persistent problems, seek specialist advice.

* Levomepromazine

Levomepromazine is available in 6mg and 6.25mg tablets, and 5mg/ml oral solution.

Dependent on the product used we would suggest an initial dose of 2.5-3.125mg, increased to 5-6.25mg if the lower dose is ineffective.

7. Emerging therapies

Treatment

- There is a growing evidence base for the role of †Olanzapine 2.5mg to 5mg orally at night in the management of systemic therapy induced nausea and vomiting, and there may be a role in other causes of nausea and vomiting. Olanzapine is also available as an orodispersible tablet.
- There is some evidence that †Mirtazepine might be effective in the management of nausea and vomiting, particularly where systemic therapy associated, and could therefore be considered where this might confer additional symptomatic benefits (e.g. mood, sleep).
- Use of isopropyl alcohol wipes for aromatherapy (inhalation) has been shown to provide acute relief of nausea.

For persistent problems, seek specialist advice.

Other management considerations

General advice

- Correct the correctable (for example renal function, hypercalcaemia, hyponatraemia, hyperglycaemia, constipation, symptomatic ascites, cerebral oedema/raised intracranial pressure, review medicines).
- Consider non-pharmacological measures (refer to non-pharmacological management below).
- Choose an anti-emetic appropriate to a likely identified cause.
- A combination of anti-emetics may be appropriate.
- A broad spectrum anti-emetic may be indicated if multiple concurrent factors are present.
- Adjuvant corticosteroid and/or benzodiazepine may be combined with the prescribed anti-emetic drug(s).
- Try to avoid the concurrent prescribing of prokinetics (for example QT metoclopramide) and anticholinergics (for example cyclizine) medication. The anticholinergics will diminish the prokinetic effect.
- Consider the route of administration of medication as:
    - the oral route may not provide adequate absorption or be available as a result of nausea (which inhibits gastric emptying) or vomiting
    - buccal or sublingual medication administration may be helpful but may trigger symptoms of nausea or vomiting in susceptible individuals
    - the parenteral route may reduce tablet burden which may be a contributing factor to nausea.

- Anti-dopaminergics should be avoided in patients with Parkinson's disease.

Non-pharmacological management

Non-pharmacological measures are important and should be considered alongside the prescribing of appropriate anti-emetics. Measures include:

- Regular mouth care (refer to Mouth care guideline)
- Reduce tablet burden where possible and consider medication formulation (for example patients may find liquid preparations or crushable tablets easier to swallow).
- Regularising bowel habit - constipation may be a relatively common cause of nausea
- Regular small palatable portions rather than large meals
- Avoid food preparation and cooking smells
- A calm and reassuring environment
- Acupressure bands (for example Seaband®)
- Acupuncture
- Psychological approaches.

Pharmacological management

Almost all causes of nausea and vomiting can be placed in the following categories, and managed using a specific drug or class of drugs.

Tables are best viewed in landscape mode on mobile devices

Causes	Drug class
Clinical toxicity (including drug induced) or metabolic/biochemical upset (refer to flowchart)	Dopamine receptor antagonist (for example metoclopramide, QT† haloperidol or QT† levomepromazine
Motility disorders (including drug-induced and paraneoplastic gastroparesis)	Prokinetic (for example metoclopramide - caution in use of prolonged higher doses, monitor for extrapyramidal side effects or QT domperidone)
Intracranial disorders, for example, vestibular dysfunction, motion disorders	Anticholinergic or antihistamine (cyclizine or † hyoscine hydrobromide), † corticosteroid, QT† levomepromazine or QT prochlorperazine.
Raised Intracranial Pressure	Corticosteroids e.g. dexamethasone

Causes	Drug class
Oral/pharyngeal/oesophageal irritation	Anticholinergic or antihistamine (cyclizine or †hyoscine hydrobromide), or QT†levomepromazine.
Multifactorial/unknown/refractory	Use appropriate anti-emetics for known causes; or broad spectrum anti-emetic QT†levomepromazine.
Higher centres (pain/fear/anxiety)	Optimise pain control treat anxiety.
Systemic therapy and/or radiotherapy-induced nausea and vomiting	Refer to local guidelines.

Practice points

- Always try to identify and treat any underlying causes of nausea and vomiting.
- Check that the most appropriate anti-emetic has been prescribed for the probable cause and is given by the most appropriate route. If nausea and vomiting persists, reassess and reconsider the possible causes and treat appropriately. If no improvement is seen, seek specialist advice.
- For persistent vomiting, assessment of hydration and nutritional status is essential and management considered in the context of the patient's clinical picture (refer to Subcutaneous fluids guideline).
- Despite logical and appropriate treatment, the patient may continue to vomit especially if there is a duodenal/gastric outflow obstruction or bowel obstruction. Remember to consider the possibility of bowel obstruction (refer to Bowel obstruction guideline).

Colicky abdominal pain after taking a prokinetic drug may suggest bowel obstruction.

Further information

Receptor site affinities

Receptor site affinities of selected anti-emetics									
	D_2 antagonist	*H_1 antagonist*	*Muscarinic antagonist*	*$5HT_2$ antagonist*	*$5HT_3$ antagonist*	*NK_1 antagonist*	*$5HT_4$ agonist*	*CB_1 agonist*	*GABA mimetic*
Domperidone[1]	**								
Haloperidol	***			*/-					
Metoclopramide[2]	**				*		**		
Cyclizine		**	**						
Hyoscine *Hydrobromide*			***						
Chlorpromazine	***	***	**	**					
Levomepromazine	**	***	**	***					
Olanzapine	**	*	**	**	*				
Prochlorperazine	***	**	*	*/**					
Promethazine	*/**	**	**						
Lorazepam									***
Nabilone								***	
Aprepitant						***			

Ondansetron/ Granisetron[3]					***				

Tables are best viewed in landscape mode on mobile devices

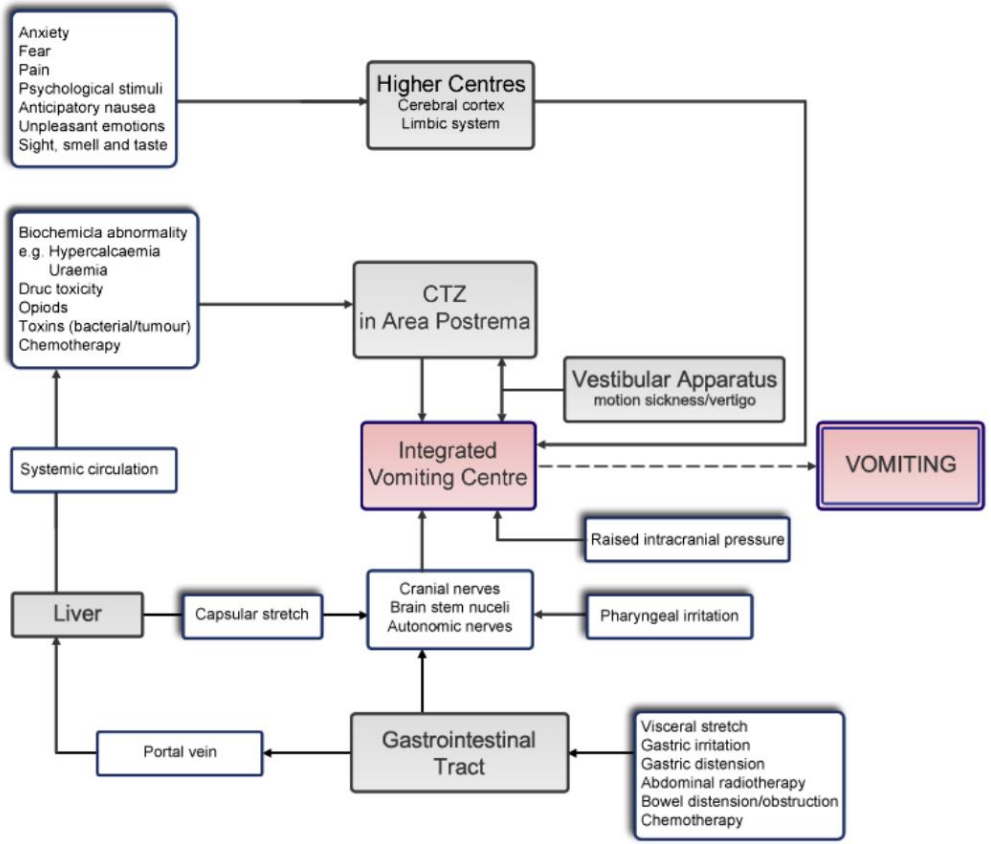
Pharmacological activity: blank = none or insignificant; * = slight; ** = moderate; *** = marked.

[1] domperidone: does not normally cross the blood-brain barrier; minimal risk of extrapyramidal effects, watch for interactions.

[2] **metoclopramide**: caution in use of prolonged higher doses, monitor for extrapyramidal side effects.
[3] **ondansetron/granisetron**: consider interactions

Adapted from Twycross, R, Wilcock, A and Howard, P (eds) Palliative Care Formulary 5th Edition 2014.

Receptor site chart



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