Nausea and Vomiting

KEY POINTS

- Nausea and vomiting are distressing symptoms, present in more than 50% of patients with advanced cancer
- Multiple receptors in the central nervous system, including dopaminergic, cholinergic, histaminic, and serotonergic receptors, are involved in the development of nausea. Blocking of these receptors forms the basis of antiemetic medications
- The choice of antiemetic therapy should be based on the presumed underlying cause of the nausea, which then identifies the receptor(s) involved and suggests the appropriate medication
- Concurrent medications from different classes may be required for effective control (e.g. **metoclopramide** and **cyclizine**, or **haloperidol** and **ondansetron**). Avoid combining more than one medication with the same pharmacological mechanism of action (e.g. metoclopramide and haloperidol) as this will cause increased side effects without improvement in symptom relief
- Corticosteroids such as dexamethasone are non-specific antiemetics and can be very helpful in certain situations (see MANAGEMENT below)

- In children with life-limiting diseases, common causes such as gastroenteritis, reflux, and infections should be considered
- Nausea and vomiting may also occur in children due to emotional distress

ASSESSMENT

See comment on page 10

- A history looking for the possible cause(s) or contributing factors can be very helpful, along with a targeted physical examination

- Select only the investigations that will alter your management plan
- Correct underlying causes of nausea and vomiting if possible and appropriate
- Causes of nausea/vomiting include:
  - Metabolic abnormalities (e.g. hypercalcaemia, liver and kidney abnormalities)
  - Medications including opioids (usually transient), chemotherapy, or antibiotics
  - Infection
  - Severe constipation and impaction
  - Gastric stasis
  - Gastrointestinal ulceration
  - Bowel obstruction (malignant and non-malignant)
  - Radiotherapy
  - Increased intracranial pressure (from brain metastases or primary brain tumours)

MANAGEMENT

Always balance the burdens of a possible intervention or treatment against the likely benefit for the patient

- Management should be "mechanism based" and reflect the most likely underlying cause of the nausea and vomiting
- Consider the best route for the medication as the oral route may not be helpful

General Measures

- Ensure good oral care, treat any signs of oral thrush
- Prevent and treat constipation

- Eliminate strong odours, keep air and room fresh
- Aromatherapy with a peppermint or ginger essential oil may reduce nausea
- Use of acupuncture or acupressure wrist bands may be beneficial
- If the cause is unknown or multifactorial, initial antiemetic medications include:
  - **Metoclopramide**: treats most common causes of nausea and vomiting, including gastric stasis and partial bowel obstruction. **Avoid in complete bowel obstruction**
  - **Haloperidol**
  - **Levomepromazine (methotrimeprazine)** has broad antiemetic activity, targeting most common receptors involved in nausea and vomiting

Opioid-Induced Nausea

- Consider a medication which has both prokinetic and antidopaminergic (e.g. **domperidone 10 mg PO/Subcutaneous/IV BID-QID**)

Gastric Stasis

- Consider a combined prokinetic and antidopaminergic (as above)

Metabolic Abnormalities or Uraemia

- Consider an antidopaminergic (e.g. **haloperidol 0.5-1 mg PO/Subcutaneous BID-TID**)
- **Olanzapine 2.5 mg PO daily or BID** is an atypical neuroleptic which blocks multiple receptors and can be useful if other options are ineffective, doses of up to 10 mg/day can be used, higher doses will cause more sedation

Gastric Irritation

- Consider any potentially emetogenic medications and adding an H2-antagonist (e.g. **famotidine 20 mg PO/Subcutaneous BID**) or a proton pump inhibitor (e.g. **omeprazole 20 mg PO daily**)

Chemotherapy or Radiation-Induced Nausea

- Consider a 5HT3 receptor antagonist, such as **ondansetron 4-8 mg q8-12h PO/IV** and/or **dexamethasone 4-8 mg qAM PO/IV/ Subcutaneous**

Motion-Induced Nausea

- Cyclizine: start with **50 mg PO BID** and **50 mg PO PRN,** titrate to **maximum of 200 mg PO daily**. If parenteral formulation available, can give **100-150 mg/24 hours via CSCI, up to 200 mg/24 hr CSCI**

Raised Intracranial Pressure

- Consider **dexamethasone 4-20 mg qAM IV/Subcutaneous or cyclizine 50 mg TID PO/IV**

Hypercalcaemia

- Consider hydration and bisphosphonates, such as **pamidronate 60-90 mg IV single dose** or **zoledronate 4 mg IV single dose**, and other specific hypercalcaemia management

Anxiety/Cortical Causes (e.g. pain, previous nausea/anticipatory nausea, emotional factors)

- Treat with benzodiazepines (e.g. **lorazepam 0.5-1 mg SL q4-12h as needed**)

Constipation

See Constipation section

Bowel Obstruction

See Malignant Bowel Obstruction section

General Management Considerations:

- Medications should be dosed regularly if nausea and vomiting are constant
- If symptoms persist, add a second or third antiemetic agent that targets different receptors
- If anxiety is a contributing factor, add a benzodiazepine (e.g. **lorazepam 0.5-2 mg q4-12h PO/Subcutaneous**) in addition to other antiemetics
- If symptoms remain persistent despite the treatments described above, then consider corticosteroids (**dexamethasone 4-8 mg daily qAM PO/Subcutaneous/IV**)

- **Metoclopramide: 0.1-0.2 mg/kg/dose PO/Subcutaneous/IV TID-QID (Maximum: 10 mg/dose, 0.5 mg/kg/day)**
- **Haloperidol initial: 0.01-0.02 mg/kg/dose PO/Subcutaneous q8-12h. Titrate to effect. (Maximum: 0.15 mg/kg/day)**
- **Famotidine (if gastritis): 0.5-1 mg/kg/dose PO daily or BID (Maximum: 40 mg/dose), or 0.25-0.5 mg/kg/dose IV daily or BID (Maximum: 20 mg/dose)**
- **Omeprazole (if gastritis) 0.7-3.5 mg/kg/dose PO daily (Maximum: 40 mg/day)**
- **Lorazepam (if anticipatory nausea and vomiting): 0.04-0.08 mg/kg/dose PO/SL x 1 dose the night before and/or morning of chemotherapy/radiation (Maximum: 2 mg/dose)**
  - **For treatment of anxiety or breakthrough nausea and vomiting): 0.05 mg/kg/dose PO/SL/IV q4-8h PRN (Maximum: 2 mg/dose)**
- **Ondansetron: 0.2 mg/kg/dose PO/IV q8-12h (Maximum: 8 mg/dose)**
- **Dexamethasone (for highly emetogenic chemotherapy or radiation): 0.15mg/kg PO/IV q6h (Maximum: 20 mg) pre-therapy q24h (lower doses recommended for moderately**

PITFALLS/CONCERNS

- In the setting of complete bowel obstruction, the use of prokinetic agents such as metoclopramide may result in increased pain and cramping and should be avoided
  - Haloperidol is a preferred option in such cases

- Metoclopramide and haloperidol (and other antidopaminergics) can cause extra pyramidal reactions in children (as well as adults), treatment with diphenhydramine (or another anticholinergic) will reduce the likelihood of this

PALLIATIVE TIPS

- For intractable nausea and vomiting, a multimodal approach combining antiemetics targeting different receptors is recommended (eg. haloperidol + dimenhydrinate (or another antihistamine) + dexamethasone)
- **Levomepromazine/methotrimeprazine** (if available) is helpful for intractable nausea since it targets most receptors involved in generating nausea and vomiting
- Ongoing nausea requires regular dosing of antiemetics rather than just "as needed" dosing
- Use non-pharmacological methods to help reduce nausea and vomiting, as well as including diet modifications (choice of foods, smaller meals) and control of odours

- Distraction, and avoiding food smells and unpleasant odours may be helpful for children

- Use caution when prescribing haloperidol, ondansetron, and metoclopramide in the setting of QTc prolongation or when patients have additional risk factors for Torsade de Pointes (e.g. hypokalaemia, hypomagnesaemia)

Nausea and Vomiting

Integrative Vomiting Centre (IVC) or Emesis Centre

Cerebral High CNS

Sensory:
Sights, smells, pain

Cerebral
Anticipatory N/V, memories, fear

Treatment:

Benzodiazepines
Cannabinoids
Relaxation therapies

Vestibular

Opioids
Cerebellar Tumor

Treatment:

H1 Antagonist
Dimenhydrinate
Methotrimeprazine

Anticholinergic
Scopolamine
Atropine

Increased Intracranial Pressure

Brain tumor - primary or metastatic

Treatment:

Dexamethasone

Treatment:

Anticholinergic
Scopolamine
Atropine

H1 Antagonist
Dimenhydrinate
Cyclizine
Methotrimeprazine

5HT2 Antagonist
Methotrimeprazine
Olanzapine

5HT3 Antagonist
Ondansetron

CB1 Antagonist
THC

NK1 Antagonist
Aprepitant

Chemoreceptor Trigger Zone (CTZ)

Drugs:
Opioids, chemotherapy

Biochemical:
Uremia, hypercalcemia

Toxic:
Septic, emetogenic peptides

Treatment:

D2 Antagonist
Phenothiazine
Haloperidol
Prochlorperazine
Methotrimeprazine
Chlorperazine

Gastrokinetic
Metoclopramide
Domperidone

5HT3 Antagonist
Ondansetron, -trons
Metoclopramide

NK1 Antagonist
Aprepitant

GI Tract - Vagal

Distension
Over-eating,stasis, extrinsic pressure

Obstruction
High,mid,low

Chemical irritants
Drugs,blood,etc.

Treatment:

D2 Antagonist
Gastrokinetic
Metoclopramide
Domperidone
Phenothiazine
Methotrimeprazine

5HT4 Agonist
Metoclopramide

5HT3 Antagonist
Ondansetron
Metoclopramide
Octreotide
Dexamethasone

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