
Antiemetics

Nausea and vomiting

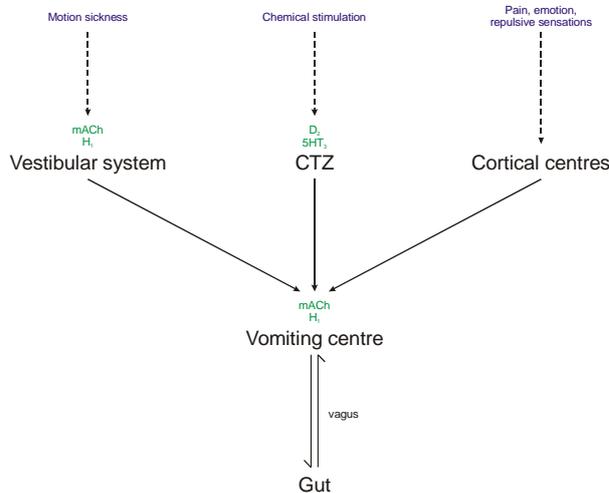
Treat cause and relieve symptoms.

Pathophysiology

The act of emesis is controlled by the vomiting centre in the medulla, which integrates afferent input from the vestibular system, the chemoreceptor trigger zone (CTZ), the cortex and the gut. The CTZ lies in the base of the fourth ventricle and is functionally outside the blood-brain barrier, and therefore responds to emetic substances in the bloodstream.

Different neurotransmitters are involved in different pathways. In a given condition, the choice of antiemetic thus depends on the transmitters in the pathway that has been activated.

Gastric stasis is often present in nausea, so consider a non-oral route for antiemetics until nausea has been absent for 24h.



Oversimplified – many other receptors are involved at each centre.

Indications

- mACH/H₁ antagonists
 - Any cause (receptors in vomiting centre are central to mechanism)
 - Particularly effective against motion sickness (action in two sites)
- D₂/5-HT₃ antagonists
 - Emetogenic substances in bloodstream, e.g. opioids, cytotoxics, uraemia

Drugs

Antimuscarinics

Hyoscine

- Mechanism
 - Central
 - Peripheral in gut – antispasmodic
- Side-effects: anticholinergic
- Clinical use: any cause

Antihistamines

Promethazine, cyclizine

- Mechanism: central
- Side-effects: sedation (less with cyclizine)
- Clinical use: any cause; less effective against substances acting on the CTZ

Antidopaminergics

Phenothiazines: chlorpromazine

- Mechanism: central (also has H₁-blocking properties)
- Side-effects: Parkinsonism, sedation (due to H₁ antagonism)
- Clinical use: any cause

Metoclopramide

- Mechanism
 - Central
 - Peripheral: enhances ACh action at muscarinic synapses in gut → increased oesophageal sphincter tone, decreased pyloric tone, increased peristalsis ('prokinetic')
- Side-effects: all antidopaminergic ones (see antipsychotics)
- Clinical use: any cause

Domperidone

- Mechanism: central
- Side-effects: less likely to cause extrapyramidal reactions than metoclopramide¹ → useful in paediatrics; hyperprolactinaemia
- Clinical use: any cause

5-HT₃ antagonists

Ondansetron, granisetron, tropisetron

- Mechanism: both peripheral and central
- Side-effects: headache, flushing, constipation
- Clinical use: chemo-/radiotherapy² (*no* role in other types of nausea caused by cancer, incl. *no* role in palliative care), post-operative nausea and vomiting
- *Very effective but highly expensive*: a single dose costs around £8, cf. 4-5p for a dose of metoclopramide or cyclizine

5-HT₂ antagonists

Levomepromazine

- Clinical use: palliative care
- Also effective against agitation

Neurokinin-1 (NK1) antagonists

- NK1 receptors are widely distributed in the brain
- An oral NK1 antagonist is licensed for chemotherapy-induced nausea

Adjuncts in chemotherapy

- Steroids – unknown mechanism
- Benzodiazepines, e.g. lorazepam – sedate

Cannabinoids

Nabilone

- Mechanism: unclear – thought to inhibit CTZ, which is antagonised by naloxone – hence an opioid-mediated effect?
- Side-effects: drowsiness, dizziness, dry mouth
- Clinical use: rare

Cisapride

Benzamide – chemically related to metoclopramide, but no antidopaminergic action. Induces ACh release from myenteric plexus, causing increased oesophageal sphincter tone and gut motility. *Not* an antiemetic. Formerly used in GORD – withdrawn as causes long QT.

¹ Poor penetration of blood-brain barrier – hence also used before commencing apomorphine in Parkinsonism to allay peripheral side-effects

² Anticancer therapy is thought to induce the release of 5-HT from enterochromaffin cells in the gut.