The management of nausea and vomiting in palliative care

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MDHB Resource nurses study day
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When did you last feel sick/vomit?

There are only two times I feel stress: day and night.
Content

- Causes of Nausea and Vomiting
- Anatomy & Physiology of Nausea and Vomiting
- Antiemetics
- Management

Objective

- Improve the management of nausea & vomiting in palliative care patients
Background

- Nausea
  - unpleasant feeling of the need to vomit
  - autonomic symptoms

- Vomiting
  - forceful expulsion of gastric contents through the mouth

- Prevalence of Nausea or Vomiting in the last year of life:
  - Advanced cancer: 40-70%
  - Non-malignant disease: 27%
Assessment/evaluation

- Distinguish between vomiting, expectoration, regurgitation
- Assess nausea and vomiting separately
  - Both or one, constant or intermittent, what relieves or exacerbates, timing of onset, associated symptoms?
  - What is the person vomiting?
- Review abdomen
- Review medications (especially for recent additions if N&V new)
- Bloods, e.g. consider—creatinine, urea, calcium, digoxin levels
Overview of the management of N&V

- Identify the cause(s) for the nausea and vomiting
- Treat reversible causes and exacerbating factors
- Rationale for anti-emetics
- Choose the appropriate route
- Review the response and, if necessary, change the management
Causes of N&V

**Chemical causes**
- Drugs: Antibiotics, NSAIDS, Steroids, Chemotherapy…
- Infection
- Metabolic stimuli:
  - Uremia,
  - Hypercalcaemia,
  - Hyponatraemia

**Gastrointestinal**
- Gastroparesis
  - Drugs
  - Paraneoplastic
- Gastric irritation/ulceration
- Hepatomegaly
- Constipation
- Ascites
- Bowel obstruction
- Chemotherapy & radiotherapy
Causes

Vestibular
- Nausea and vomiting worse on movement
- May be associated with
  - cranial nerve lesions
  - base of skull metastases

Raised intracranial pressure
- Cerebral tumours
- Trauma
- Hydrocephalus
Causes

Oropharangeal

- Regurgitation
- Cough
- Poor oral hygiene
- Oral infection
  - ‘gag reflex’
<table>
<thead>
<tr>
<th>Causes</th>
<th>Characteristics</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vestibular</td>
<td>Exacerbated by movement</td>
<td>Medications: cyclizine, Scopoderm patch</td>
</tr>
<tr>
<td>Obstruction</td>
<td>Constipation, Mechanical obstruction – vomiting with abdominal pain and distension</td>
<td>Clear bowel, Evaluate for surgery or radiation, Supportive care – graseby syringe driver with buscopan and cyclizine</td>
</tr>
<tr>
<td>Motility</td>
<td>Upper GI stasis or dysmotility – caused by tumour, drugs eg: morphine, TCA’s</td>
<td>Metoclopramide orally or subcutaneously Metoclopramide or haloperidol if opioid induced</td>
</tr>
<tr>
<td>Infection</td>
<td>Viral gastroenteritis or bowel infection, Systemic infection, Cerebral metastases</td>
<td>Antibiotics, Cyclizine, Dexamethasone, Cyclizine</td>
</tr>
<tr>
<td>Intracranial pressure raised</td>
<td>Worse in morning, Projectile vomiting, Worse on head movement</td>
<td></td>
</tr>
<tr>
<td>Toxins</td>
<td>Drugs, Metabolic eg; hypercalcaemia and uraemia, Toxic from hepatic or renal failure, Constant nausea, Variable vomiting</td>
<td>Haloperidol, Metoclopramide</td>
</tr>
</tbody>
</table>
Central Pathways: Vomiting centre

- **Vomiting centre** – lies close to area postrema but within blood brain barrier.
- **Coordinates** the emetic process, receiving and integrating input from various sources.
  - **Higher centres** – fear, anxiety, memory, pain...
  - **Chemoreceptor trigger zone** – drugs, metabolic disturbances, sepsis..
  - **Vestibular stimulation**
  - **Raised inter-cranial pressure**
  - **Gastro intestinal** - Vagal afferents (chemo & mechano receptors liver, gut viscera/serosae: head neck thorax abdomen)
STOMACH AND SMALL INTESTINE

BLOOD-BORNE EMETICS
Chemotherapy Opioids Ipecac

SENSORY INPUT
Sight Smell Pain

HIGHER CENTERS
Anticipation Fear Memory

VOMITING CENTER

VOMITING via output to stomach, diaphragm, and abdominal muscles

Receptors

5HT = Serotonin
DA = Dopamine
M = Muscarinic cholinergic
H1 = Histamine1
INNER EAR/PHARYNX
Receptors: ACh, Histamine1, 5HT2

STOMACH
Mechano and chemoreceptors: D2, 5HT4, 5HT3

CHEMORCEPTOR TRIGGER ZONE
Receptors: Dopamine D2, 5HT3

LIVER
Mechano and chemoreceptors: 5HT3, 5HT4, D2

BOWEL
Mechano and chemoreceptors: 5HT3, 5HT4, D2
# Receptor site affinities of antiemetics

<table>
<thead>
<tr>
<th></th>
<th>Dopamine D&lt;sub&gt;2&lt;/sub&gt;-antagonist</th>
<th>Histamine H&lt;sub&gt;1&lt;/sub&gt;-antagonist</th>
<th>Acetylcholine (muscarinic) antagonist</th>
<th>5HT&lt;sub&gt;2&lt;/sub&gt;-antagonist</th>
<th>5HT&lt;sub&gt;3&lt;/sub&gt;-antagonist (serotonin)</th>
<th>5HT&lt;sub&gt;4&lt;/sub&gt;-antagonist</th>
</tr>
</thead>
<tbody>
<tr>
<td>Metoclopramide&lt;sup&gt;a&lt;/sup&gt;</td>
<td>++</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>(+)</td>
<td>++</td>
</tr>
<tr>
<td>Domperidone&lt;sup&gt;a&lt;/sup&gt;</td>
<td>++</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
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<tr>
<td>Ondansetron</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>+++</td>
<td>0</td>
</tr>
<tr>
<td>Cyclizine</td>
<td>0</td>
<td>++</td>
<td>++</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Hyoscine hydrobromide (Scopoderm™)</td>
<td>0</td>
<td>0</td>
<td>+++</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Haloperidol&lt;sup&gt;b&lt;/sup&gt;</td>
<td>+++</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Levomepromazine&lt;sup&gt;c&lt;/sup&gt; (Nozinan)</td>
<td>++</td>
<td>+++</td>
<td>++</td>
<td>+++</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Olanzapine</td>
<td>+</td>
<td>+++</td>
<td>+</td>
<td>+++</td>
<td>present</td>
<td></td>
</tr>
</tbody>
</table>

**Pharmacological activity:** 0 none or insignificant, + slight, ++ moderate, +++ marked

a. **Domperidone & Metoclopramide** both have prokinetic activity and encourage gastric emptying. Metoclopramide crosses the blood-brain barrier and exerts a central effect but may cause dystonic reactions, decreased mental acuity and drowsiness. Domperidone may therefore be a better option for patients who are on antidepressants, anti-psychotics or the elderly.

b. **Haloperidol** 1.5 – 3mg nocte is the drug of choice for ‘chemically’ induced nausea including that caused by opioids.

c. **Levomepromazine** 6.25mg nocte PO, has affinities for several receptor sites and is a good first line broad spectrum anti-emetic. May be sedating.
Management

Non-drug measures

- Dietary changes
- Reduce food smells
- Calm environment
- Smaller meals
- Smaller plates
- Salty, sweet taste changes
Management

Correct reversible causes

- Cough - antitussive
- Gastritis – reduce gastric acid (e.g. antacid, PPI)
- Consider stopping gastric irritant drugs (e.g. NSAIDs)
- Constipation – laxatives
- Raised intracranial pressure – corticosteroids
- Hypercalcaemia - bisphosphonate
Correct reversible causes

- Raised intracranial pressure
  - Dexamethasone and radiotherapy

- Hypercalcaemia
  - Rehydration and bisphosphonates

- Anxiety and emotional distress
  - Benzodiazepines and counselling
The Anti-Emetics

Dopamine antagonists
- Haloperidol
- Levomepromazine
- Metaclopramide
- Domperidone

Mode of action
- Blocks dopamine receptors – acts on CTZ

Side-effects (Parkinson like)
- Muscle stiffness
- Tremor
- Reduced movements
The Anti-Emetics (2)

Histamine antagonists
- Cyclizine
- Levomepromazine

Mode of action
- Blocks histamine receptors – vomiting centre

Side-effects
- Drowsiness
- Anticholinergic i.e. dry mouth
The Anti-Emetics (3)

Antimuscarinic

- Hyoscine Hydrobromide (Scopaderm TTS)
- Hyoscine Butylbromide (Buscopan) - anti-secretory

Mode of action
Antagonises the action of acetycholine - usually at receptor site – vomiting centre

Side-effects
- Dry mouth
- Sedation
- Stuffy nose
The Anti–Emetics (4)

- **Dopamine antagonists** (prokinetic)
  - Metoclopramide
  - Domperidone

- **Mode of action** - prokinetic
  - 5HT4 agonist
  - Dopamine antagonist (gut wall and centrally)

- **Side effects**
  - Severe dystonic reactions oculogyic crisis (metoclopramide)
  - Less risk of extrapyramidal effects with Domperidone
The Anti-Emetics (5)

- Serotonin antagonists (5HT3 antagonists)
  - Ondansetron

- Mode of action
  - Blocks 5HT3 from activating the vagus
  - The vagus is down-regulated, reducing stimulation to CTZ

- Issues
  - Role unclear in palliative care
  - Use in ‘acute emesis’ post chemotherapy

- Side effects
  - Constipation
Additional Drugs

- Steroids: can potentiate anti-emetics
- Benzodiazepines
- Octreotide
- Proton pump inhibitors e.g. omeprazole or pantoprazole
Prescribing an appropriate anti-emetic

Be guided by probable cause of N&V in relation to mechanism of action of the drug

- Give regularly
- Parenteral route necessary if PO absorption compromised
  - Stat dose parentally
  - Consider continuous subcutaneous infusion
- Suppositories
Anti-Emetics

- Optimise the dose every 24 hours
- After 24-48 hours, if little or no benefit on optimum doses:
  - Do you have the correct cause?
    - No: change to an appropriate anti-emetic
    - Yes: add in or substitute another anti-emetic
- Most anti-emetics can be given SC (not domperidone)
- Doses generally the same if given PO, SC, IV
- Avoid combinations with antagonistic actions (eg cyclizine and metoclopramide)
- If you need to combine – complementary (eg cyclizine and haloperidol)
Indeterminate

- Levomepromazine (Nozinan)
- Haloperidol and/or Cyclizine
- Consider: Metoclopramide
- Dexamethasone
Case study: Mrs Brown 78yrs

- Admitted to ARC – 3months ago.
- History of metastatic breast cancer, multiple bone and liver metastases. GP has recently started morphine elixir 2.5mg to 5mgs q4hly.
- Today she tells you she just doesn’t feel like breakfast – she feels ‘seedy’.
- What do you want to ask her?
- What additional information would be helpful?
Two months later

- She reports a bad headache, she says she has been getting them in the morning lately and they are getting worse.
- When you go to help her out of bed she stops you because she feels sick.

- What might be the cause of her headache?
- Her nausea?
In a ‘nutshell’

- Cause(s)
- Right drug(s)
- Non pharmacological

- Some patients will continue to have
  - Nausea
  - Vomiting