Nausea & Vomiting in advance cancer - Revisit

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Nausea & vomiting are common symptoms in advance cancer, affecting between 40 – 70% of patients.

NAUSEA
Nausea is an unpleasant feeling of the need to vomit. It is often accompanied by autonomic symptoms – such as pallor, cold sweat, salivation, tachycardia, and diarrhea. It is usually associated with changes in gut motility patterns, especially gastric stasis. Gastric acid secretion is reduced & salivation increased. Nausea is usually more prolonged & more difficult to control than vomit.

VOMITING
Vomiting is defined as forceful expulsion of the gastric contents via the mouth. It is commonly followed by lethargy & pronounced muscular weakness.

ANATOMY & PHYSIOLOGY (FIG 1 &2)
Stress, anxiety & nausea from any cause induce delayed gastric emptying (via peripheral dopaminergic R on myenteric plexus). This effect is antagonized by the D2-receptor antagonists eg. Metoclopramide & domperidone. In GI tract, enterochromaffin cells in bowel wall is rich in 5HT, which is massively release in response to various stimuli: abdominal RT, chemotherapy & bowel distention and sensitizes the vagal nerve which terminate in CTZ.

Fig. 1. Major emetogenic pathways
MANAGEMENT OF NAUSEA & VOMITING

- Evaluation
- Explanation to patient & family
- Individualized treatment
- Supervision & monitoring
- Attention to Detail

EVALUATION – Identify the most likely cause(s)- (usually caused by several concurrent factors) through detailed history, physical examination, investigation (if appropriate).

1. **Detailed History**-
   It is important to distinguish between vomiting & expectoration (by check the pH: gastric secretions – acidic; expectorate – alkaline). Try to evaluate nausea & vomiting separately. Find out the time of onset of symptoms e.g. coinciding with the patient starting morphine. Review drug regimen. Review pattern of vomiting –
   - Diurnal variation, related to meal time
   - Whether nausea is absent or persistent for prolonged periods after vomiting

Note the content of vomitus - **color**: coffee ground, bile, blood stained, undigested food; **odour**: faeculent. Search for factors which may affect or exacerbate the symptoms of N & V: pain & fear, anxiety, odours: e.g. from fungating wound.

2. Physical examination

3. Investigation if appropriate

1. **Common causes of Nausea & Vomiting in advance Cancer**
   - Metabolic - Hypercalcaemia, renal failure
   - Toxic
   - RT, Chemotherapy, infection or paraneoplastic phenomenon
2. Record the severity of symptoms

3. Correct reversible causes -
   Potentially reversible causes & exacerbating factors should be treated when appropriate – eg. severe pain, infection, cough, hypercalcaemia, tense ascites

4. Non-drug treatments - General measures including:
   - A calm, reassuring environment with fresh air
   - Unpleasant odors should be minimized e.g. Colostomy, fungating tumour or decubitus ulcer
   - Avoidance of exposure to foods known to precipitate N & V
   - Avoidance of perfumes, odors of foods that may precipitate N & V
   - Sour foods such as lemons & rinsing of mouth with weak lemon juice may reduce nausea
   - Small portions, small snacks (esp. for pts with anorexia & early satiety)
   - Distraction – talk, music, TV, radio & reading may be of assistance

5. Start drug treatment with an antiemetic if Steps 3 & 4 will not give immediate relief

   **First-line antiemetics:**
   - **Prokinetic antiemetic:** for gastritis, gastric stasis, functional bowel obstruction
     Eg. Metoclopramide
   - **Antiemetic (act in CTZ):** for most chemical causes of vomiting eg. Morphine, Eg. Haloperidol
   - **Antiemetic (act in VC):** for mechanical bowel obstruction, - ICP, motion sickness
     Eg. cyclizine

   **Do not prescribe a prokinetic drug & an anticholinergic drug concurrently**
   - The final common pathway for prokinetic drugs is cholinergic
   - Anticholinergic drugs (include cyclizine) block their prokinetic action

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**Table 1 Receptor site affinities of selected antiemetics**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dopamine D² antagonist</th>
<th>Histamine H¹ antagonist</th>
<th>Acetylcholine (muscarinic) antagonist</th>
<th>5HT₃ antagonist</th>
<th>5HT⁴ antagonist</th>
<th>5HT₆ antagonist</th>
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<tbody>
<tr>
<td>Metoclopramide</td>
<td>++</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>++</td>
</tr>
<tr>
<td>Domperidone</td>
<td>++⁺</td>
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<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
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<td>Clonidine</td>
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<td>0</td>
<td>0</td>
<td>0</td>
<td>+++</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 butylbromide</td>
<td>0</td>
<td>0</td>
<td>+++</td>
<td>0</td>
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<td>0</td>
</tr>
<tr>
<td>Haloperidol</td>
<td>+++</td>
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<td>0</td>
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<td>0</td>
</tr>
<tr>
<td>Prochlorperazine</td>
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<tr>
<td>Chlorpromazine</td>
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<tr>
<td>Levomepromazine</td>
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<td>+++</td>
<td>++</td>
<td>+++</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

**Pharmacological activity:** 0 none or insignificant, + slight, ++ moderate, +++ marked.
- a. Domperidone does not cross the blood-brain barrier and therefore does not cause extrapyramidal effects.
- b. Other 5HT antagonists – e.g. granisetron and tropisetron – have comparable receptor affinity.

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- a. Domperidone does not cross the blood brain barrier and therefore does not cause extrapyramidal effects.
Important factors to consider when prescribing for N & V

- Take account of the effects of antiemetics on GI motility
  - Prokinetic (metoclopramide, domperidone)
  - Antikinetic (anticholinergics, antihistaminic anticholinergics)
- Adjuvant use of antisecretory drugs (eg hyoscine butylbromide, octreotide)
- Use of corticosteroids
- Use of appropriate administration route that ensures delivery of the antiemetic to the site of action
- Appropriate treatment of psychological factors (counselling, benzodiazepines)
- Adverse effects of drugs
- Costs of drugs

6. Re-evaluate at regular intervals
- Optimise the dose of antiemetic every 24 hours
- Change the treatment if there is no improvement after 24 – 48 hours
- Add an appropriate 2nd antiemetic on a 24-48 hour trial basis (~ 1/3 of pts with N&V need >1 antiemetic for satisfactory control)

Explanation
Explain the cause of N & V & discuss the treatment options with patient & the family
Which in turn will enable the patient to maintain some element of control

References