NAUSEA & VOMITING

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Nausea and Vomiting

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Disclosure Information

Joseph W. Shega, MD
Has no relevant financial relationship to disclose

Acknowledgement
Gordon Wood, MD

Objectives
• Assessment
• Pathophysiology
• Treatment
  – Mechanism
  – Empiric
Case: Mr. Q

- 50 year old electronics designer with esophageal cancer metastatic to liver
- Third-line palliative chemotherapy (capecitabine)
- PMH: migraines, depression, ulcerative colitis as child
- Esophageal stent and J tube for feeding

Case: Mr. Q

- Intermittent N/V through course of chemo
- Worse after starting capecitabine 10 days prior to admission
- Painful burning sensation in chest
- Bilious vomit 10x/day and dry heaves
- No relation to feedings
- Normal daily bowel movements
- Ondansetron not effective at home

Case: Mr. Q

- Antiemetics: ondansetron, scopolamine, lorazepam, promethazine
- Other meds: Morphine, bupropion, potassium, fentanyl
- Normal exam and labs
- No change abdomen/pelvis CT (no dilated bowel loops)
Mechanism-Based Therapy

1. Careful assessment to determine etiology
2. Use knowledge of pathophysiology to determine receptors underlying symptoms
3. Choose antiemetic to block implicated receptors

Epidemiology in Palliative Care

- 62% of all terminal cancer patients with 40% in last 6 weeks of life1
- 71% of patients admitted to a palliative care unit2
- 25% of pain consults3
- Undertreated: 39% hospitalized cancer patients with nausea got antiemetic4

Evaluation

- History
  - Characterize N/V
  - Associated Symptoms
  - Medication history
  - Prior therapies
  - Past medical history
- Physical examination

Evaluation

• Laboratory Testing

• Radiology

Evaluation

• Confident in cause of N/V in 45 of 61 hospice patients
• Chemical abnormalities 33% (metabolic, drugs, infection)
• Impaired gastric emptying 44%
• Visceral and serosal causes 31% (bowel obstruction, GI bleed, enteritis, constipation)


Evaluation

• 40 patient episodes of nausea and/or vomiting on inpatient palliative care unit
• 59 reversible etiologies
  – 51% medications
  – 19% constipation


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Mr. Q

- Esophageal burning
- Esophageal stent placement
- Chemotherapy (capecitabine)
- Opioid therapy (morphine and fentanyl)
- Bupropion and Potassium
- Esophageal irritation from cancer
- Liver mets
- Migraines, ulcerative colitis

Mechanism-Based Therapy

1. Careful assessment to determine etiology
2. Use knowledge of pathophysiology to determine receptors underlying symptoms
3. Choose antiemetic to block implicated receptors

Mechanism: The 4 Pathways

1. Chemoreceptor Trigger Zone
2. Cortex
3. Peripheral Pathways
4. Vestibular System

Wood GJ, Shega JW, Lynch B, Von Roenn JH. Management of intractable nausea and vomiting in patients at the end of life: “I was feeling nauseous all of the time... nothing was working.” JAMA. 2007;298(10):1196-1207
Mechanism-Based Therapy

1. Careful assessment to determine etiology
2. Use knowledge of pathophysiology to determine receptors underlying symptoms
3. Choose antiemetic to block implicated receptors

Mr. Q

- Esophageal irritation due to tumor and reflux $\rightarrow$ Achm and H1 in Peripheral Pathways
- Opioids $\rightarrow$ D2 in CTZ
- Chemotherapy $\rightarrow$ NK1 in CTZ and 5HT3 in GI tract and CTZ
### Antiemetics

<table>
<thead>
<tr>
<th>Antiemetic</th>
<th>Receptor Antagonized</th>
</tr>
</thead>
<tbody>
<tr>
<td>Metoclopramide (PO, IV, and sub q)</td>
<td>D2 (GI tract)</td>
</tr>
<tr>
<td></td>
<td>5HT3 (at high doses)</td>
</tr>
<tr>
<td>Haloperidol (PO, IV, IM, sub Q)</td>
<td>D2 (CTZ)</td>
</tr>
<tr>
<td>Prochlorperazine (PO, IV, rectal)</td>
<td>D2 (CTZ)</td>
</tr>
<tr>
<td>Chlorpromazine (PO, IV, IM, rectal)</td>
<td>D2 (CTZ)</td>
</tr>
<tr>
<td>Promethazine (PO, IV, rectal)</td>
<td>H1, Achm, D2 (CTZ)</td>
</tr>
</tbody>
</table>


### Antiemetics: Continued

<table>
<thead>
<tr>
<th>Antiemetic</th>
<th>Receptor Antagonized</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diphenhydramine (PO, IV, Sub Q)</td>
<td>H1</td>
</tr>
<tr>
<td>Scopolamine (PO, patch, gel)</td>
<td>Achm</td>
</tr>
<tr>
<td>Hyoscyamine (SubL, PO, Sub Q, IV)</td>
<td>Achm</td>
</tr>
<tr>
<td>Ondansetron (PO, IV)</td>
<td>5HT3</td>
</tr>
<tr>
<td>Mirtazapine (PO)</td>
<td>5HT3</td>
</tr>
</tbody>
</table>


### Haloperidol (and D2’s in general)

- No well-designed RCT’s evaluating use for nausea and vomiting in palliative care
  - Substantial clinical experience supports its use
  - Ample evidence in other settings
  - Low cost
  - Cardiovascular and cerebrovascular risks
    - Risks versus benefits
    - Counsel families

2. Buttner M et al. Anesthesiology 2005 101(8) 1454-1463

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**5HT3 Antagonists**

- Effective for:
  - Chemotherapy-induced N/V
  - Radiation therapy-induced N/V
  - Post-operative N/V
  - Smaller studies suggest efficacy for nausea due to opioids or uremia

- Otherwise, no more effective than cheaper D2 antagonists for most common causes of N/V


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**Opioid Induced Nausea and Vomiting**

- **CINV prophylaxis**
  - Needles
    - Reduces acute emesis
    - No reduction acute or delayed nausea
    - Electroacupuncture has greatest effect
  - Acupressure
    - Reduces acute nausea severity but not acute vomiting

- **Post-operative nausea and vomiting**
  - P6 acupressure superior to placebo in preventing early nausea and vomiting, but not late vomiting

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**Acupuncture-Point Stimulation**

- **CINV prophylaxis**
  - Needles
    - Reduces acute emesis
    - No reduction acute or delayed nausea
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- **Post-operative nausea and vomiting**
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Mechanism-Based Therapy

- 40 patient episodes of N/V in inpatient palliative care unit
- Most common causes: gastric stasis/outlet obstruction (35%), chemical/metabolic (30%)
- Nausea resolved in 28 of 34 cases (82%)
- Vomited resolved in 26 of 31 cases (84%)
- Total symptom control in mean of 3.4 days


Empiric Treatment

- Mechanism-based therapy effective1,2
- Some advocate empiric D2 antagonists3 in all cases
- No head-to-head comparison
- D2 antagonists are our first choice in acutely symptomatic patients undergoing workup


Benefits of mechanism-based therapy

- Potentially more effective in certain scenarios
- Facilitates systematic approach that identifies all possible contributors
- Guides treatment of underlying causes
- Informs choices of second and third antiemetics
- Minimizes risks of side-effects and over medicating
Nonpharmacological Therapy

- Avoid strong smells or other triggers
- Small, frequent meals
- Limit oral intake during severe episodes
- Relaxation techniques
- Acupuncture and acupressure including wrist bands (P6 stimulation)\(^1\)


Refractory/Intractable N/V

- Schedule around-the-clock
- Add second agent to block other implicated receptors
- Prophylactic dosing
- Treat underlying cause if possible

Summary

**Mechanism-based approach**

- Careful assessment to determine etiology
- Use knowledge of pathophysiology to determine receptors underlying symptoms
- Choose antiemetic to block implicated receptors
- Also treat underlying etiology
Nausea and Vomiting

References


