Nausea, Vomiting, Bowel Obstruction

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Coleman Palliative Care Intensive
February 13, 2015
Objectives

- Describe a three step approach to the management of N/V at the end of life
- Identify strategies to manage refractory N/V in persons near the end of life
- Describe how to medically manage a malignant bowel obstruction
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-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
Evaluation

- History
- Physical examination

...think “Head-to-Toe”
Evaluation

• Laboratory Testing
  – What labs should you consider?

• Radiology
  – What imaging should you consider?
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
  – 11% constipation

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
Mechanism: The 4 Pathways

Sensory input
- Anxiety
- Meningeal irritation
- Increased intracranial pressure

Motion
- Labyrinth disorders

Drugs
- Metabolic products
- Bacterial toxins

Mechanical stretch
- (e.g., GI obstruction or stasis)
- GI mucosal injury (e.g., metastases, candida infection, GERD, radiation therapy, chemotherapy)
- Local toxins and drugs

Mechanism:

- Achm H₁
- Vestibular system

Projections from vestibular nuclei

- D₂ (central)
- 5HT₃
- NK₁

Chemoreceptor trigger zone

Intracerebral projections

Vagus and splanchnic nerves

- Vagus, splanchnic, and glossopharyngeal nerves, sympathetic ganglia

Peripheral pathways

- 5HT₃ receptors in GI tract
- Mechanoreceptors and chemoreceptors in GI tract, serosa, and viscera

Input

Neuroreceptors

Neural pathways

Nausea/Vomiting

Drugs
Metabolic products
Bacterial toxins

Mechanical stretch
(eg, GI obstruction or stasis)
GI mucosal injury (eg, metastases, candida infection, GERD, radiation therapy, chemotherapy)
Local toxins and drugs

Projections from vestibular nuclei

$D_2$ (central)
$5HT_3$
$NK_1$

Chemoreceptor trigger zone

Vagus and splanchnic nerves

$5HT_3$ receptors in GI tract
Mechanoreceptors and chemoreceptors in GI tract, serosa, and viscera

Peripheral pathways
Sensory input
Anxiety
Meningeal imitation
Increased intracranial pressure

Intracerebral projections

Chemoreceptor trigger zone

Achm
$H_1$
$5HT_2$

Vomiting center

Nausea/Vomiting
Mechanism: The 4 Pathways

- **Sensory input**
  - Anxiety
  - Meningeal irritation
  - Increased intracranial pressure

- **Motion**
  - Labyrinth disorders

- **Drugs**
  - Metabolic products
  - Bacterial toxins

- **Mechanical stretch**
  - (e.g., GI obstruction or stasis)
  - GI mucosal injury (e.g., metastases, candida infection, GERD, radiation therapy, chemotherapy)
  - Local toxins and drugs

- **Peripheral pathways**
  - 5HT3 receptors in GI tract
  - Mechanoreceptors and chemoreceptors in GI tract, serosa, and viscera

- **Input**

- **Neuroreceptors**

- **Neural pathways**

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
# Antiemetics

<table>
<thead>
<tr>
<th>Antiemetic</th>
<th>Receptor Anagonized</th>
</tr>
</thead>
<tbody>
<tr>
<td>Metoclopramide (Reglan)</td>
<td>?</td>
</tr>
<tr>
<td>Haloperidol (Haldol)</td>
<td>?</td>
</tr>
<tr>
<td>Prochlorperazine (Compazine)</td>
<td>?</td>
</tr>
<tr>
<td>Chlorpromazine (Thorazine)</td>
<td>?</td>
</tr>
<tr>
<td>Promethazine (Phenergan)</td>
<td>?</td>
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</table>

# Antiemetics: Continued

<table>
<thead>
<tr>
<th>Antiemetic</th>
<th>Receptor Anatagonized</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diphenhydramine (Benadryl)</td>
<td>?</td>
</tr>
<tr>
<td>Scopolamine (Transderm Scop)</td>
<td>?</td>
</tr>
<tr>
<td>Hyoscyamine (Levsin)</td>
<td>?</td>
</tr>
<tr>
<td>Ondansetron (Zofran)</td>
<td>?</td>
</tr>
<tr>
<td>Mirtazapine (Remeron)</td>
<td>?</td>
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</tbody>
</table>

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%)
- Vomiting resolved in 26 of 31 cases (84%)
- Total symptom control in mean of 3.4 days

Empiric Treatment

- Mechanism-based therapy effective\(^1,^2\)
- Some advocate empiric D2 antagonists\(^3\) 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
Opioid-induced Nausea and Vomiting

Opioid-induced Nausea and Vomiting

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Opioid-induced Nausea and Vomiting

Metoclopramide
Haloperidol
Prochlorperazine

Opioid-Induced N/V

• D2 antagonists first-line
• Generally resolves within 3-5 days of continued use
• 10-20% dose reduction may alleviate nausea without loss of analgesia¹
• Opioid rotation also effective²

Chemotherapy-induced nausea and vomiting

Chemotherapy-induced nausea and vomiting

Chemotherapy-induced nausea and vomiting

Chemotherapy-induced nausea and vomiting

Chemotherapy-induced nausea and vomiting

Ondansetron
Dexamethasone
Aprepitant

Impaired GI Motility

Motion
Labyrinth disorders

Drugs
Metabolic products
Bacterial toxins

Mechanical stretch
(eg, GI obstruction or stasis)
GI mucosal injury (eg, metastases, candida infection, GERD, radiation therapy, chemotherapy)
Local toxins and drugs

Sensory input
Anxiety
Meningeal irritation
Increased intracranial pressure

Vestibular system

D₂ (central)
5HT₃
NK₁

Chemoreceptor trigger zone

Vagus and splanchnic nerves
Vagus, splanchnic, and glossopharyngeal nerves, sympathetic ganglia

Peripheral pathways

5HT₃ receptors in GI tract
Mechanoreceptors and chemoreceptors in GI tract, serosa, and viscera

Achm
H₁

Cortex

Intracerebral projections

Achm
H₁
5HT₂

Vomiting center

Nausea/Vomiting

Impaired GI Motility

Sensory input
- Anxiety
- Meningeal irritation
- Increased intracranial pressure

Motion
- Labyrinth disorders

Drugs
- Metabolic products
- Bacterial toxins

Mechanical stretch
- (e.g., GI obstruction or stasis)
- GI mucosal injury (e.g., metastases, candida infection, GERD, radiation therapy, chemotherapy)
- Local toxins and drugs

Achm $H_1$
- Vestibular system

D$_2$ (central)
- 5HT$_3$
- NK$_1$

Projections from vestibular nuclei

Chemoreceptor trigger zone
- Intracerebral projections
- Vagus and splanchnic nerves
- Vagus, splanchnic, and glossopharyngeal nerves, sympathetic ganglia

Achm $H_1$
- 5HT$_2$

Vomiting center

Nausea/Vomiting

5HT$_3$ receptors
- in GI tract

Mechanoreceptors and chemoreceptors
- in GI tract, serosa, and viscera

Peripheral pathways

Impaired GI Motility

Metoclopramide

5HT3 receptors in GI tract
Mechanoreceptors and chemoreceptors in GI tract, serosa, and viscera

Input
Neuroreceptors
Peripheral pathways

Mechanical stretch (eg, GI obstruction or stasis)
GI mucosal injury (eg, metastases, candida infection, GERD, radiation therapy, chemotherapy)
Local toxins and drugs

Sensory input
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Projections from vestibular nuclei

Cortex

Intracerebral projections

D2 (central) 5HT3 NK1
Chemoreceptor trigger zone

Intracerebral projections

Achm H1 5HT2
Vomiting center

Nausea/Vomiting

Radiation-associated N/V

- Motion
  - Labyrinth disorders

- Drugs
  - Metabolic products
  - Bacterial toxins

- Mechanical stretch
  - (e.g., GI obstruction or stasis)
  - GI mucosal injury (e.g., metastases, candida infection, GERD, radiation therapy, chemotherapy)
  - Local toxins and drugs

- 5HT3 receptors in GI tract
  - Mechanoreceptors and chemoreceptors in GI tract, serosa, and viscera

- Peripheral pathways

- 5HT2 receptors

- Sensory input
  - Anxiety
  - Meningeal irritation
  - Increased intracranial pressure

- Intracerebral projections

- D2 (central) 5HT3 NK1
  - Projections from vestibular nuclei

- Chemoreceptor trigger zone
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- Achm H1
  - Intracerebral projections

- Vomiting center
  - Nausea/Vomiting

- Cortex

Radiation-associated N/V

Radiation-associated N/V

5HT3 antagonists

Brain Tumor

Motion
Labyrinth disorders

Sensory input
Anxiety
Meningeal irritation
Increased intracranial pressure

Cortex

Vestibular system

Achm
$H_1$

Projections from vestibular nuclei

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$H_1$
$5HT_2$

Nausea/Vomiting

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Peripheral pathways

Mechanical stretch (eg, GI obstruction or stasis)
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Local toxins and drugs

Drugs
Metabolic products
Bacterial toxins

Motion-associated N/V

Motion
Labyrinth disorders

Sensory input
Anxiety
Meningeal irritation
Increased intracranial pressure

Motion
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Peripheral pathways

Vagus, splanchnic, and glossopharyngeal nerves, sympathetic ganglia

Motion-associated N/V

Motion-associated N/V

Scopolamine
Diphenhydramine
Promethazine

Malignant Bowel Obstruction

Malignant Bowel Obstruction

Malignant Bowel Obstruction

Malignant Bowel Obstruction

Metoclopramide
Haloperidol
Dexamethasone

Motion
Labyrinth disorders

Sensory input
Anxiety
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Vestibular nuclei

Projections from

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Vomiting center

Nausea/Vomiting

Malignant Bowel Obstruction

• Most common in ovarian, colorectal CA

• Interventional management
  – Surgery if prognosis > 2 mos
  – Stent, NG tubes, venting PEG tubes

• Medical Management
  – Analgesic: opioid
  – Antisecretory: Octreotide/anticholinergic
  – Antiemetic: Metoclopramide/haloperidol
  – Steroid: Dexamethasone
Nonpharmacological Therapy

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

Refractory/Intractable N/V
Refractory/Intractable N/V

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

• Less traditional agents
  – Dexamethasone (Decadron)
  – Mirtazapine (Remeron)
  – Dronabinol (Marinol)
  – Olanzapine (Zyprexa)
  – Megestrol (Megace)
  – Thalidomide (Thalomid)
5HT3 Antagonists

• Effective for:
  – Chemotherapy-induced N/V\(^1\)
  – Radiation therapy-induced N/V\(^2\)
  – Post-operative N/V\(^3\)
  – Smaller studies suggest efficacy for nausea due to opioids\(^4\) or uremia\(^5\)

• Otherwise, no more effective than cheaper D2 antagonists for most common causes of N/V\(^6\)

Polypharmacy

- Most anti-emetics are centrally active
- Mechanism-based therapy prevents use of multiple medications antagonizing same receptor
Conclusions

1. 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

2. Refractory/Intractable N/V
   • Multiple agents, around-the-clock and prophylactically
   • Less traditional agents
Questions?