AAHPM

American Academy of
Hospice and Palliative Medicine

NAUSEA & VOMITING

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AAHPM Intensive Board Review Course

Nausea and Vomiting

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Disclosure Information

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

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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 life[1]
- 71% of patients admitted to a palliative care unit[2]
- 25% of pain consults[3]
- Undertreated: 39% hospitalized cancer patients with nausea got antiemetic[4]

1. Reuben DB et al. Arch Intern Med. 1986;146(10):2021-2023
2. Fainsinger R et al. J Palliat Care. 1991;7(1):5-11.
3. Meuser T et al. Pain. 2001;93(3):247-257.
4. Greaves et al. Support Care Cancer 2009;17(4):461-464

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)

Stephenson J et al. Support Care Cancer. 2006;14(4)348-353.

Evaluation

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

Bentley A et al. Palliat Med. 2001;15(3):247-253

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
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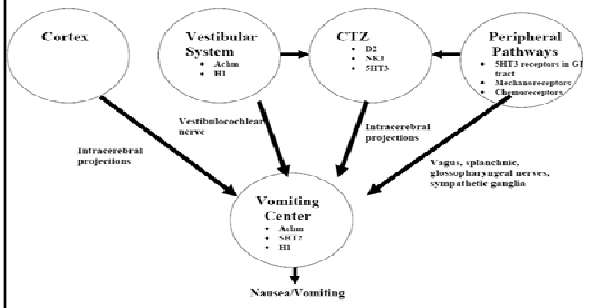
Mechanism: The 4 Pathways

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

Pathways



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

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Mr. Q

- Esophageal irritation due to tumor and reflux → Achm and H1 in Peripheral Pathways
- Opioids → D2 in CTZ
- Chemotherapy → NK1 in CTZ and 5HT3 in GI tract and CTZ

Antiemetics

Antiemetic	Receptor Anatagonized
Metoclopramide (PO, IV, and sub q)	D2 (GI tract) 5HT3 (at high doses)
Haloperidol (PO, IV, IM, sub Q)	D2 (CTZ)
Prochlorperazine (PO, IV, rectal)	D2 (CTZ)
Chlorpromazine (PO, IV, IM, rectal)	D2 (CTZ)
Promethazine (PO, IV, rectal)	H1, Achm, D2 (CTZ)

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

Antiemetics: Continued

Antiemetic	Receptor Antagonized
Diphenhydramine (PO, IV, Sub Q)	H1
Scopolamine (PO, patch, gel)	Achm
Hyoscyamine (SubL, PO, Sub Q, IV)	Achm
Ondansetron (PO, IV)	5HT3
Mirtazapine (PO)	5HT3

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

Haloperidol (and D2's in general)

- No well-designed RCT's evaluating use for nausea and vomiting in palliative care[1]
  - Substantial clinical experience supports its use
  - Ample evidence in other settings[2]
  - Low cost
  - Cardiovascular and cerebrovascular risks[3]
    - Risks versus benefits
    - Counsel families

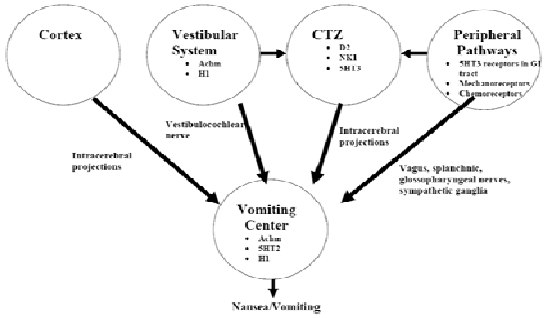
1. Perkins et al. Cochrane Database Syst Rev 2009
2. Buttner M et al. Anesthesiology 2005 101(6) 1454-1463
3. Ray WA et al. N Engl J Med 2009 360 (3): 225-235

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]

1. Kris MG et al. J Clin Oncol. 2006;24(18):2932-2947.
2. Roberts JT et al. Oncology. 1993;50(3)173-179.
3. Gan TJ et al. Anesth Analg. 2003;97(1):62-71.
4. Sussman G et al. Clin Ther. 1999;21(7)1216-1227.
5. Ljutic D et al. Kidney Blood Press Res. 2002;25(1)61-64.
6. Weschules DJ et al. Am J Hosp Palliat Care. 2006;23(2):135-149.

Opioid Induced Nausea and Vomiting



Wood, G. J. et al. JAMA 2007;298:1196-1207.

Acupuncture-Point Stimulation

- 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 accupressure superior to placebo in preventing early nausea and vomiting, but not late vomiting

Naeim, A. et al *JCO* 2008;*26*(23). 3903-3910
Nunley et al. Journal of PeriAnesthesia Nursing 2008 23(4):247-261

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

Bentley A et al. Palliat Med. 2001;15(3):247-253

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

1. Stephenson J et al. Support Care Cancer. 2006;14(4)348-353.
2. Lichter I et al. J Palliat Care. 1993;9(2):19-21.
3. Bruera E et al. J Pain Symptom Manage. 1996;11(3):147-153.

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]

1. Vickers AJ. J R Soc Med. 1996;89(6):303-311.

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

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2. Billio, A., Morello, E., Clarke, M.J. (2010) Serotonin receptor antagonists for highly emetogenic chemotherapy in adults. *Cochrane Database of Systemic Reviews,* Issue 1. Art. No.: CD006272. DOI: 10.1002/14651858.CD006272.pub2.

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6. Wood, G.J., Shega, J.W., Lynch, B., Von Roenn, J.H. (2007). Management of intractable nausea and vomiting in patients at the end of life. *Journal of the American Medical Association 298*(10). 1196-1207.