Overview of nausea and vomiting

Understanding, assessing, and managing nausea and vomiting, common symptoms in hospice and palliative care patients

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Objectives

1. Learn the NAUSEA acronym to assess patients with nausea and vomiting
2. Learn the VOMIT acronym to identify common causes of vomiting
3. Understand why it is important to match the treatment of nausea and vomiting to the cause(s) of nausea and vomiting
Disclosure

- Amanda Sommerfeldt, MD, has no potential or actual conflicts of interest to disclose.
- Off-label use of medications, particularly haloperidol, will be discussed during this presentation.
- Subcutaneous administration of some anti-emetic medications is done routinely in practice, but has not been well-studied and is not recommended by the manufacturers of these medications.
- Patient care is individualized. Always seek guidance from an experienced and knowledgeable physician and/or pharmacist if you have questions or concerns about medication dose, frequency, or route of administration.

What is “nausea”?

- Unpleasant sensation vaguely referred to the epigastrium and abdomen, with a tendency to vomit. (Dorland’s Medical Dictionary)
- Origin is the Greek word naus (“ship”) — Refers to the seasickness experienced by sailors — nausia in Greek, and nausea in Latin.
What does it mean to “vomit”?

• To eject stomach contents through the mouth
  (Dorland’s Medical Dictionary)
  – Origin is the Latin word vomere ("spew forth", “discharge”)
• Medical term for vomit is “emesis”
  – From the Greek word emein (“to vomit”)

Related terminology

• Retching
  – “Dry heaves”
  – Same mechanism as vomiting, but glottis in back of throat stays closed, so stomach contents aren’t expelled
• Regurgitation
  – Small amounts of food return to the mouth due to a blockage in the esophagus, an esophageal motility problem, or GERD
• Rumination
  – Food in the stomach is returned to the mouth and then swallowed again
  – No nausea
How common are nausea and vomiting?

- 70-85% of pregnant women
  - Usually in the first 9 weeks of pregnancy
  - Most severe form is hyperemesis gravidarum (up to 2% of pregnant women)
- 90-100% of patients receiving total-body irradiation
  - Most common with radiation to abdomen, pelvis, or mantle
  - Least likely with breast, extremities, or brain
- 40-60% of patients with advanced cancer
  - 71% with ovarian cancer
  - Up to 55% still have N&V in last 4 weeks of life

What’s so bad about N&V?

- Diminished quality of life
  - Uncomfortable or distressing to patient
  - Upsetting to friends and family
  - Takes away from enjoyment of meals and can contribute to weight loss
- Nausea and vomiting can be symptoms of a serious underlying problem
Important point:

Nausea and vomiting are symptoms of a diagnosis. They are not the diagnosis.

Why is it so hard to treat N&V?

• Patients and families don’t always report the symptoms
  – Some patients with cancer think that it is normal and expected to have N&V
  – Perception may be that it is untreatable
• Failure to identify the cause of N&V
  – Not recognizing medications that cause or contribute to N&V
  – Not realizing that a patient is pregnant, has a brain tumor, is constipated, etc.
Why is it so hard to treat N&V?

• Using the wrong anti-emetic medication
  – Failure to match the treatment to the cause
  – Using multiple anti-emetics with similar mechanisms of action
    • Prochlorperazine and haloperidol
    • Granisetron and ondansetron
  – Failure to recognize that the cause of N&V can change over time
    • Cancer patient who had chemo in the past now has N&V due to constipation

Why is it so hard to treat N&V?

• Wrong dose
  – Not giving the anti-emetic medication often enough
  – Not increasing the doses of anti-emetic medications when appropriate
• Inappropriate route of administration
  – Giving oral meds to someone who can’t swallow or who is continuously vomiting
  – Giving rectal meds to someone with frequent diarrhea
How to successfully manage nausea and vomiting
(in 3 easy steps)

1. Assess the patient
   • History
   • Physical examination

2. Identify the cause(s) of the N&V, if possible

3. Direct treatment toward the cause
   • Fix the cause when possible
   • Medications
   • Non-pharmacologic measures

Step 1:
Assessment of nausea and vomiting

Remember N-A-U-S-E-A
Assessment of N&V

- **Nausea history and intensity**
  - Rating on 0-10 intensity scale
  - Description and duration of symptoms
  - Previous experiences with nausea and vomiting

- **Aggravating factors**
  - Certain foods, eating, drinking, not eating, medications, movement, time of day

- **Quality of life**
  - How upsetting is this?

Assessment of N&V

- **Symptoms associated with the nausea/vomiting**
  - Dizziness, fatigue, sweating, pain, constipation, diarrhea, fever, weight loss, anxiety, depression, etc.

- **Emetic episodes per 24 hour period**

- **Alleviating factors**
  - What helps?
    - Medications, distraction, food, vomiting
Examining the patient with N&V

• Appearance
  – Sick or well?
  – Distressed or calm?
  – Pale? Jaundiced?

• Skin and mucous membranes
  – Sweaty, excess salivation
  – Can see skin tenting and dry mouth with dehydration

Examining the patient with N&V

• Abdominal exam
  – Tenderness
  – Distention
  – Fluid wave to suggest ascites
  – Masses – tumor, stool, bladder
  – Bowel sounds

• May need a rectal exam if constipated
Step 2: Identify the cause(s) of the nausea and vomiting
Remember V-O-M-I-T

The major players

1. GI tract
2. Vestibular apparatus
   • Part of the inner ear that senses motion and body position
3. Chemoreceptor Trigger Zone (CTZ)
   • Area postrema on the floor of the 4th ventricle
   • Located in the dorsal medulla (brainstem)
   • Loose blood-brain barrier
   • Chemicals in the bloodstream and CSF can affect the CTZ
4. Cerebral cortex
   • Taste, sight, smell, memory, and emotion can stimulate or suppress nausea and vomiting
What makes a person vomit?

GI tract → CTZ

Vestibular apparatus

Emetic Center
nucleus tractus solitarius in the medulla

Cerebral cortex

Receptors involved

GI tract
S-HT3, also M1, H1, NK1

Vestibular apparatus
H1, M1

Emetic Center
M1

CTZ
D2, S-HT3, also M1, H1, NK1

Cerebral cortex
Nausea and vomiting occur when the GI tract, CTZ, cerebral cortex, and/or vestibular apparatus signal the Emetic Center to trigger vomiting.

V - Vestibular

- Motion sickness, BPPV, Meniere’s disease, tumor, infection affecting inner ear (labyrinth)
- Visual cues can also trigger nausea
O – Obstruction of bowel

- Constipation, ileus (slowed bowel), partial or complete bowel obstruction
- Think of a clogged water pipe

| Blocked intestinal flow | Dilation of bowel before the blockage and decompression of bowel past the blockage | Increases in bowel lumen pressure, bowel wall edema, fluid secretion, and peristalsis | Release of ACh, histamine, +/- serotonin | Activation of the Emetic Center | Emesis |

M – Motility problems in the upper gut

- Medical conditions
  - Diabetes, AIDS, scleroderma, small cell lung cancer, cirrhosis, pancreatic cancer, gastroenteritis, GERD, hypo/hyperthyroidism, neurologic disorders (CVA, ALS, Parkinson’s)
- Psychiatric disorders and rumination syndrome
- Medications like opioids, lithium, nicotine, CCBs, clonidine, TCAs, some chemotherapies
- Iatrogenic
  - Radiation, injury to vagus nerve during surgery
M - Motility problems in the upper gut

- Medical condition, medication, or injury to vagus nerve
- Interruption of electrical and/or mechanical processes that regulate stomach contractions
- Release of dopamine, serotonin, histamine, ACh, +/- substance P
- Activation of the CTZ, or direct activation of the Emetic Center
- Emesis

I – Infection/Inflammation

- Bacterial toxins, viral infections, meningitis, encephalitis
- Brain tumor, concussion, stroke
T - Toxins

• Metabolic disorders
  – DKA, uremia, low oxygen, elevated calcium
  – Estrogen release of pregnancy

• Drugs
  – Sinemet, estrogen, opioids (D2 mediated), chemotherapy, digoxin, nicotine, general anesthetics, ergot alkaloids

Toxin → Release of dopamine +/- serotonin → Activation of the CTZ → Activation of the Emetic Center → Emesis

Step 3:
Direct treatment toward the cause of the N&V

Fix when possible.
Palliate when fix is not possible or not feasible.
General management principles

• Treat the underlying cause if possible
• If constipated, consider benefits and burdens of a laxative regimen
  – Senna acts by stimulating the myenteric plexus in the GI tract
• Some anti-emetic medications can be used to treat other symptoms as well
  – Agitation
  – Anxiety
  – Secretions

General management principles

• May need more than one medication
  – Avoid using multiple medications with similar mechanisms of action
• Limited data to support the efficacy of the medications used
  – Case reports
  – Small studies
    • Usually cancer patients receiving chemotherapy
Classes of anti-emetic medications

1. Anticholinergic (acetylcholine blockers)
2. Anti-dopaminergic (dopamine blockers)
3. 5-HT3 antagonists (serotonin blockers)
4. Antihistamines (histamine blockers)
5. Other
   - Corticosteroids
   - Cannabinoids
   - Benzodiazepines
   - Novel drugs

Anticholinergics

- Mechanism of action
  - Block acetylcholine (ACh) at muscarinic (M1) receptors

- Drugs
  - Scopolamine patch – TD
  - Hyoscynamine – SL, PO
  - Meclizine (Antivert) – PO
    • Also acts as an antihistamine
Anticholinergics

• Useful for
  – Vestibular N&V
    • Motion sickness
    • Room-spinning dizziness, inner ear problems
• Side effects and risks
  – Sedation or confusion, especially in elderly or very ill
  – Dry mouth, blurred vision, tachycardia, dizziness, flushing, urinary retention

Anti-dopaminergics

• Mechanism of action
  – Block dopamine at D2 receptors
  – Metoclopramide also acts as a pro-kinetic
• 3 classes of drugs
• Useful for
  – N&V due to opioids, electrolyte imbalances, migraine, CTZ activation, or unknown cause
  – Dual purpose if patient also has agitation, delirium, or psychosis
  – Metoclopramide specifically for upper GI motility disorders
Classes of dopamine blockers

1. Phenothiazines
   • Prochlorperazine (Compazine) – PO, PR, IV
   • Chlorpromazine (Thorazine) – PO, IV, IM
   • Perphenazine (Trilafon) – PO

2. Butyrophenones
   • Haloperidol (Haldol) – PO, IV, IM, SC
   • Droperidol (Inapsine) – IM/IV only

3. Substituted benzamide
   • Metoclopramide (Reglan) – PO, IV

Risks and side effects of dopamine blockers

• Common side effects
  – Sedation, dizziness, dry mouth
  – Haloperidol is less sedating

• Rare, more serious side effects
  – Extrapyramidal symptoms
    • Tremor, movement disorders
  – Tardive dyskinesia
    • Repetitive, involuntary movements like lip smacking
  – QT prolongation / arrhythmia
    • Associated with haloperidol and droperidol
    • Continuous EKG recommended with droperidol
Contraindications to using dopamine blockers

- Parkinson’s disease and related conditions
  - Increased risk of dopamine depletion leading to EPS or tardive dyskinesia
- Movement disorders
- Caution if prolonged QT, heart disease, history of arrhythmia, dementia, elderly, history of seizures

5-HT3 antagonists

- Mechanism of action
  - Block serotonin at 5-HT3 receptors
- Drugs
  - Ondansetron (Zofran) – PO, IV
  - Granisetron (Kytril, Sancuso) – PO, IV, TD
  - Dolasetron (Anzemet) – PO, IV
- Useful for
  - Most data for chemotherapy-induced N&V
  - Prevent post-op emesis or emesis from radiation
  - Can use for N&V due to opioids and some other toxins
Serotonin blockers

• Side effects and risks
  – Headache, dizziness, itching, urinary retention, constipation, diarrhea
  – Elevated liver enzymes
  – Extrapyramidal symptoms (EPS) – rare
  – QT prolongation (rare)

Antihistamines

• Mechanism of action
  – Block histamine at H1 receptors
  – Many also block acetylcholine (anticholinergic)

• Drugs
  – Promethazine (Phenergan) – PO, PR, IV, IM
  – Dimenhydrinate (Dramamine) – PO, IV
  – Diphenhydramine (Benadryl) – PO, IV

▶ Newer antihistamines like loratadine (Claritin) and fexofenadine (Allegra) do not cross the BBB and are not useful treatments for N&V
Histamine blockers

• Useful for
  – Vestibular N&V
  – Patients who also have nasal allergies, congestion, URI, or insomnia

• Side effects and risks
  – Sedation, blurred vision, dizziness, dry mouth, urinary retention, confusion (especially elderly)
  – Extravasation risk (IV > IM)

Other anti-emetic medications
Corticosteroids

• Mechanism of action
  – Unclear
  – May block release of arachidonic acid
• Drugs
  – Dexamethasone (Decadron) – PO, IV, IM
  – Methylprednisolone (Medrol) – PO, IV, IM
• Useful for
  – N&V due to inflammation, chemotherapy, unknown cause
  – Patients who also have anorexia or fatigue
• Side effects and risks
  – Fluid retention/edema, insomnia, agitation, psychosis, adrenal insufficiency, hyperglycemia, immunosuppression, bone loss

Cannabinoids

• Mechanism of action
  – Affect cannabinoid receptors near the Emetic Center
• Drugs
  – Dronabinol (Marinol) – PO
• Useful for
  – Advanced HIV/AIDS
  – Better tolerated and works better for younger patients or patients who previously benefited from Marinol or marijuana
• Side effects and risks
  – Sedation, dizziness, agitation, hallucinations, seizures
Benzodiazepines

- **Mechanism of action**
  - Enhances the effects of GABA by binding to benzodiazepine receptors in the brain
- **Drugs**
  - Lorazepam (Ativan) – PO, IV, IM, SC
- **Useful for**
  - Anticipatory or vestibular N&V
  - Associated anxiety or insomnia
- **Side effects and risks**
  - Sedation, dry mouth, dizziness, paradoxical agitation, abuse, dependence

Novel anti-emetics

- **Aprepitant (Emend)**
  - Blocks Substance P at NK-1 receptors
  - Used with dexamethasone and serotonin blockers to prevent delayed CINV
  - Very expensive!
- **Olanzapine (Zyprexa)**
  - Atypical antipsychotic that blocks dopamine, serotonin, and histamine
  - Used for N&V caused by opioids or CINV
  - Also used for refractory N&V in advanced cancer
  - More expensive and sedating compared with haloperidol
Cost considerations

- Haloperidol 1 mg
  - $20 for #90
- Prochlorperazine 5 mg
  - $14 for #30
- Metoclopramide 10 mg
  - $17 for #90
- Ondansetron 8 mg
  - $40 for #30
- Scopolamine 1.5 mg patch
  - $69 for #4
- Dronabinol 5 mg
  - $679.93 for #60

What do I do if I have no idea what is causing the nausea and vomiting?

Think safety, efficacy, and cost-effectiveness
Treatment recommendations when cause of N&V is not known

- Haloperidol
- Prochlorperazine
- Metoclopramide
- Dexamethasone

Non pharmacologic measures

- Mainly anecdotal evidence
- Ask and educate
  - Uncover hidden fears about what the N&V means
  - Many patients assume it is normal to not move bowels if patient is not eating (it’s not!)
  - Review what is possible in terms of N&V management
  - Review diet
    - Might try small, more frequent meals
    - Low fat diet and avoidance of non-digestible fiber if early satiety or delayed gastric emptying
Non-pharmacologic measures

• Ginger
  – May help nausea/vomiting in early pregnancy or motion sickness
  – Animal studies show benefit for CINV

• Acupuncture
  – Some efficacy for treating CINV and post-op N&V

• Cognitive behavioral therapies (CBT)
  – May help prevent cortical N&V

Non-pharmacologic measures

• Progressive muscle relaxation and guided imagery may help prevent CINV

• Hypnosis
  – May help reduce N&V, early satiety, and anxiety
  – To work, patient must be able to concentrate

• Other measures tried
  – Distraction
  – Systematic desensitization
  – Music therapy
Conclusions

1. Nausea and vomiting are common symptoms that are associated with a variety of medical conditions.
2. N&V can adversely impact quality of life in a number of ways.
3. The NAUSEA acronym can be used to aid in the assessment of patients with N&V.

Conclusions

4. The VOMIT acronym can be used to quickly recall common causes of N&V.
5. Management of nausea and vomiting is most likely to succeed when the treatment is matched to the cause.
6. Haloperidol is a cost-effective medication that can be used to manage N&V due to a variety of causes, but it is not appropriate for all patients or in all circumstances.
References / Further Reading


References / Further Reading

Thank you!

Questions? Comments? Concerns?