

Approach to Nausea and Vomiting

By

James F. Graumlich, MD, FACP
Associate Professor of Medicine and Clinical Pharmacology
University of Illinois College of Medicine
Peoria, IL 61637

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Objectives:

At the end of this session, the learner will be able to

- List the causes of nausea and vomiting based on organ systems
- Describe the diagnostic approach to nausea and vomiting based on the history and physical exam and diagnostic laboratory and radiographic tests
- Discuss the pharmacologic interventions available for the treatment of nausea and vomiting
- Describe interventions to prevent complications of nausea and vomiting

References:

- Gan TJ. Postoperative nausea and vomiting--can it be eliminated? *JAMA*. 287(10): 1233-6, 2002 Mar 13.
- Tramer MR. A rational approach to the control of postoperative nausea and vomiting: evidence from systematic reviews. Part II. Recommendations for prevention and treatment, and research agenda. *Acta Anaesthesiologica Scandinavica*. 45(1): 14-9, 2001 Jan.
- Apfel CC, Korttila K, Abdalla M, Kerger H, Turan A, Vedder I, Zernak C, Danner K, Jokela R, Pocock SJ, Trenkler S, Kredel M, Biedler A, Sessler DI, Roewer N; IMPACT Investigators. A factorial trial of six interventions for the prevention of postoperative nausea and vomiting. *N Engl J Med*. 2004 Jun 10;350(24):2441-51.

Case Discussion

A 35 year old woman with history of type I diabetes came to the Emergency Department with a 3 day history of nausea and vomiting associated with some epigastric abdominal pain. The entire episode started after her recent discharge from the hospital after a total abdominal hysterectomy. Her medications included insulin, ramipril, aspirin and oxycodone. The only new medicine prescription was oxycodone for treatment of post-operative pain.

- 1) *Discuss the various etiologies for nausea and vomiting.*
- 2) *How can history help with differential diagnosis of a patient presenting with nausea and vomiting?*
- 3) *How can physical exam help with the differential diagnosis and management of a patient with nausea and vomiting?*
- 4) *What are the complications associated with nausea and vomiting?*
- 5) *What are the pharmacologic agents available for the management of nausea and vomiting?*

1) Discuss the various etiologies for nausea and vomiting.

The etiologies of nausea and vomiting exist in several broad categories.

1a. Disorders of the gastrointestinal tract and related organs, including

- Acute abdominal emergencies
- Appendicitis
- Cholecystitis
- Intestinal obstruction (adhesions, malignancy, hernia, volvulus)
- Peritonitis
- Hepatitis
- Pancreatitis
- Biliary disease
- Peptic ulcer disease (vomit during eating)
- Decreased gastrointestinal motility
- Postvagotomy syndrome
- Diabetic autonomic neuropathy
- Aerophagia
- Bacterial overgrowth syndrome

1b. Infectious diseases, including

- Numerous gastrointestinal infections
- Numerous systemic infections

1c. Disorders of the Central Nervous System, including

- Increased intracranial pressure (Neoplasm, encephalitis, hydrocephalus)
- Vertigo

- Meniere's disease
- Labyrinthitis
- Motion sickness
- Migraine
- Tabes
- Meningitis
- Syncope

1d. Disorders of the cardiovascular system, including

- Myocardial infarction
- Heart failure with passive congestion of the liver

1e. Metabolic disorders, including

- Uremia
- Diabetic ketoacidosis
- Hypo- or hyper-parathyroidism
- Hyperthyroidism
- Adrenal insufficiency
- Morning sickness
- Hyperemesis gravidarum = pregnancy plus morning sickness plus fluid-electrolyte abnormalities

1f. Drug adverse effects, including

- Opioid
- General anesthesia
- Digoxin
- Non Steroidal Anti-Inflammatory Drug (NSAID)
- Theophylline
- Ipecac
- Cytotoxic chemotherapy

1g. Toxins, including

- Food poisoning toxin
- Alcohol (early morning vomit)

1h. Psychiatric, including

- Bulimia
- Psychogenic vomiting (small volume vomit, weight usually maintained)

2) How can history help with differential diagnosis of a patient presenting with nausea and vomiting?

History can be very helpful in the differential diagnosis of a patient with nausea and vomiting.

- Feculent vomit
 - Suggests distal intestinal obstruction, gastrocolic fistula, peritonitis
- Biliious vomit
 - Suggests prolonged vomiting, occasionally obstruction distal to ampulla Vater
- Vomiting undigested food 4-6 hours after ingestion
 - Suggests pyloric obstruction, gastroparesis, achalasia, Zenker's diverticulum
- Relief of abdominal pain with vomit
 - Suggests peptic ulcer
- Vomit during eating
 - Suggests peptic ulcer
- Early satiety with vomiting
 - Suggests gastroparesis
- Projectile vomiting sometimes without antecedent nausea
 - Suggests increased intracranial pressure
- Early morning vomit
 - Suggests alcoholism or uremia
- Chronic (longer than one month) small volume vomit, weight usually maintained
 - Suggests psychogenic vomiting
- Missed menses
 - Suggests morning sickness from pregnancy
- Abnormal CAGE questions
 - Suggests alcoholic gastritis, pancreatitis
- Vertigo
 - Suggests etiologies involving central nervous system, cranial nerve VIII

3) *How can physical exam help with the differential diagnosis and management of a patient with nausea and vomiting?*

- Orthostatic deterioration of pulse and blood pressure
 - Suggests intravascular volume depletion that will require therapy with intravenous fluids to prevent organ failure
- Absent jugular venous pulsation
 - Suggests intravascular volume depletion that will require therapy with intravenous fluids to prevent organ failure
- Dry mucous membranes
 - Suggests dehydration that may require therapy with intravenous fluids to prevent organ failure
- Any abnormality of the abdomen exam
 - Suggests disorders of the gastrointestinal tract and related organs (see above for differential diagnosis)
- Papilledema, nystagmus, or focal neurological deficit

- Suggests disorders of the Central Nervous System (see above for differential diagnosis)

The following diagnostic tests will help in the differential diagnosis of nausea and vomiting after a detailed history and physical.

- Pregnancy test
- Electrolytes
- Renal function test
- Liver function tests
- Lipase
- Abdomen radiograph may help to diagnose obstruction or ileus or stones
- Stool for occult blood may help to diagnose bleeding ulcer
- Electrocardiogram
- Brain imaging tests are reserved for patients with suggestive history and neurologic exams

4) *What are the complications associated with nausea and vomiting? What complications may require the services of a consultant?*

What are the complications of nausea and vomiting?

- Dehydration
- Metabolic alkalosis
- Hypokalemia
- Malnutrition
- Vitamin, mineral deficiencies
- Dental caries
- Aspiration pneumonitis if concomitant coma
- Pressure rupture of esophagus (Boerhaave's syndrome)
- Mallory-Weiss syndrome
 - Linear mucosal tears in cardio-esophageal junction with hematemesis

The complications that may require the services of a consultant include:

- Aspiration pneumonitis may require mechanical ventilation and the services of a pulmonary consultant.
- Esophageal rupture requires the services of a thoracic surgeon.
- Mallory-Weiss syndrome requires the diagnostic services of a gastrointestinal endoscopist.

5) *What are the pharmacologic agents available for the management of nausea and vomiting?*

- The most effective therapy is to treat or eliminate the underlying cause of nausea and vomiting.
- If the patient has bowel obstruction, then naso-gastric tube drainage may relieve nausea and vomiting while awaiting definitive treatment of obstruction.
- If the patient receives an opioid analgesic, then a dose reduction or a change to another opioid may reduce nausea and vomiting. A non-opioid adjuvant analgesic like acetaminophen or NSAID may treat pain while causing a dose-sparing effect on opioid use.
- If the patient has gastritis from NSAID, then therapy with a proton pump inhibitor (omeprazole and others) may relieve nausea and vomiting.
- If therapy of the underlying etiology does not relieve nausea and vomiting, then there are several classes of antiemetic drugs to try.
 - a) *Serotonin antagonists*
 - b) *Dopamine antagonists*
 - c) *Corticosteroids*
 - d) *Benzodiazepines*
 - e) *Histamine (H1) antagonists*
 - f) *Antimuscuranic drugs*

4a. Serotonin antagonists

- Ondansetron
- Dolasetron
- Granisetron
- Tropisetron
- Palonosetron

4b. Dopamine antagonists

- Promethazine
- Prochlorperazine
- Metoclopramide

Tips for prescribing dopamine antagonists:

Prescription: Promethazine 25mg intramuscular every 6 hours as needed for nausea or vomiting

Prescription: Promethazine 25mg by rectum every 6 hours as needed for nausea or vomiting

Prescription: Prochlorperazine 10mg by mouth every 6 hours as needed for nausea or vomiting. (Maximum of 40mg/24 hours)

Prescription: Prochlorperazine 25mg by rectum every 12 hours as needed for nausea or vomiting

Prescription: Metoclopramide 10mg intravenous every 6 hours as needed for nausea or vomiting

Higher doses and repeat doses of dopamine antagonists may increase antiemetic efficacy. Watch out for dystonia and other extrapyramidal adverse effects when prescribing dopamine antagonists.

There is no rationale for prescribing two or more dopamine antagonists as combination therapy.

If nausea and vomiting persist after the first dose of dopamine antagonist, then prescribe another antiemetic drug from a different pharmacologic class, e.g., ondansetron and/or dexamethasone.

4c. Corticosteroid

- Dexamethasone

Tips for prescribing dexamethasone:

Prescription: Dexamethasone 8mg intravenous times one dose as needed for nausea or vomiting

Higher doses of dexamethasone are NOT known to increase efficacy.

If nausea and vomiting persist after the first dose of dexamethasone, then prescribe another antiemetic drug from a different pharmacologic class, e.g., dopamine antagonist and/or ondansetron.

Watch out for hyperglycemia as an adverse effect of dexamethasone.

4d. Benzodiazepine

- Lorazepam

Lorazepam has a limited role in the management of nausea and vomiting that does not respond to therapy with ondansetron plus dopamine antagonist plus dexamethasone.

4e. Histamine-H1-antagonists

- Diphenhydramine
- Meclizine
- Hydroxyzine

Histamine-H1-antagonists have a limited role in the management of nausea and vomiting caused by vestibular disorders, for example, motion sickness.

4f. Antimuscarinic drugs

- Scopolamine
Scopolamine has a limited role in the management of nausea and vomiting caused by vestibular disorders, for example, motion sickness.

Case continued.....

Additional history elements and review of systems were non-contributory.

Physical examination revealed supine blood pressure 110/80 mm Hg, supine pulse 96 beats per minute; Standing blood pressure 88/74 mm Hg, standing pulse 120 beats per minute.

Oral mucosa was dry. Jugular veins were flat. Cardiac and pulmonary exams were normal. The abdominal was soft without distension. The hysterectomy incision showed appropriate healing without inflammation or tenderness. There was no mass or organomegaly. Bowel sounds were normal. The neurological exam revealed no papilledema and no focal deficits. Rectal exam was normal tone with heme negative stool.

6) Based on the above history and physical, what differential diagnosis would you consider in this patient?

The differential diagnosis for nausea and vomiting in this patient includes

- Adverse effect of opioid, oxycodone
- Post-operative infection: abscess, wound infection
- Diabetic ketoacidosis
- Gastritis secondary to aspirin
- Angioedema of the abdomen secondary to angiotensin converting enzyme inhibitor, ramipril
- Diabetic gastroparesis
- Pancreatitis
- Hepatitis
- Pregnancy

7) What further diagnostic tests would you consider in this patient?

Laboratory tests

- Pregnancy test
- Electrolytes
- Renal function test
- Liver function tests
- Lipase

Case Continued.....

Her laboratory tests revealed; Sodium of 132, K 4.5, chloride 88, bicarbonate of 29, BUN of 35, creatinine of 1.0, blood glucose of 200. Her liver enzymes and lipase levels were within normal limits. Pregnancy test was negative. Her WBC count was 8,800, Hgb-12.4, Hct 38.4 and platelet count of 256,000.

8) How would you approach the management of this patient?

Identification of underlying complications and their treatment

This patient has volume depletion and dehydration as a complication of her prolonged nausea and vomiting, so in addition to identifying and treating the underlying cause of her nausea and vomiting, one also needs to volume resuscitate this patient.

Her initial orders should include:

- Measure and record vital signs per protocol
- Measure and record intake and output per protocol
- Measure and record capillary glucose every 4 hours
- Measure and record weight once
- Activity: bedrest, may use bathroom with assistance
- Diet: NPO except medications
- Intravenous fluids: Normal saline one liter at 500 mL per hour; then volume resuscitation should be continued based on your assessment of her volume status.

Identify and treat the underlying cause:

- This patient has received an opioid analgesic, then a dose reduction or a change to another opioid may reduce nausea and vomiting. A non-opioid adjuvant analgesic like acetaminophen or NSAID may treat pain while causing a dose-sparing effect on opioid use.

Treatment of nausea and vomiting

- Prescription: Ondansetron 4mg intravenous once
- If nausea and vomiting persist after the first dose of ondansetron, then give
- Prescription: Metoclopramide 10mg intravenous every 6 hours as needed for nausea or vomiting
- Plan to avoid dexamethasone because of risk of hyperglycemia in this patient with diabetes mellitus.

Section II

For each of the following clinical situations select an appropriate anti-emetic medication that can be used for the as the first line of treatment.

- a) A 75 year old female with history of hypertension and osteoporosis presents to the emergency room with acute onset of vertigo associated with severe nausea and vomiting. After a detailed evaluation in the emergency room she was diagnosed with acute labyrinthitis

Answer:

Antihistamines such as meclizine, dimenhydrinate are useful anti-emetic in patients with migraine, motion sickness and vertigo

- b) A 45 year old female is admitted to the oncology floor for her second round of chemotherapy for Hodgkin's Lymphoma. You receive a call from the nurse that the patient has severe nausea and requests some medications for relief of her symptoms.

Answer:

Serotonin 5-hydroxytryptamine antagonists: Ondansetron (Zofran), Dolasetron, Granisetron, Tropisetron and Palonosetron

The other agents that have been found to be beneficial in post chemotherapy nausea and vomiting are corticosteroids (dexamethasone), and promethazine, phenothiazines. If the patient does not respond to the treatment with Ondansetron, dexamethasone and promethazine then benzodiazepines can be used as an adjunct therapy for chemotherapy related symptoms

- c) You are called at midnight by the nurse in a surgical unit a request for medications for a patient's nausea and vomiting. Patient is a 55 year old male who was admitted to the hospital for total knee replacement. Post-operatively patient was started on a morphine PCA. Patient is hemodynamically stable and has no other complaints. Physical exam is unchanged from the previous documented note on the chart.

Answer:

Decrease the dose or discontinue morphine. This might help alleviate the symptoms of nausea and vomiting. A non-opioid adjuvant analgesic like acetaminophen or NSAID may treat pain while causing a dose-sparing effect on opioid use.

The following tips apply to patients with post-operative nausea and vomiting and may be generalized to other patients with nausea and vomiting. These tips do NOT apply to chemotherapy-induced nausea and vomiting. Prescription: Ondansetron 4mg intravenous once or twice daily as needed for nausea and vomiting, Prescription: Ondansetron 8mg by mouth once or twice daily as needed for nausea and vomiting

If nausea and vomiting persist after the first dose of ondansetron, then a second dose provides NO additional benefit. Higher doses of ondansetron are NOT known to increase efficacy except when treating chemotherapy-induced nausea and vomiting. Dolasetron, granisetron, tropisetron, and palonosetron have similar efficacy and toxicity when compared to ondansetron. There is no rationale to switch to another serotonin antagonist if ondansetron fails.

If nausea and vomiting persist after the first dose of ondansetron, then prescribe another antiemetic drug from a different pharmacologic class, e.g., dopamine antagonist and/or dexamethasone.

- d) A 65 year old female with history of diabetes mellitus is being evaluated by her primary care provider for nausea of one month duration that has been steadily worsening in intensity. As a part of her diagnostic evaluation, she underwent gastric emptying studies that shows delayed gastric emptying and gastroparesis. She presents to your office for the management of her nausea.

Answer:

Prescription: Metoclopramide; Higher doses and repeat doses of dopamine antagonists may increase antiemetic efficacy. Watch out for dystonia and other extrapyramidal adverse effects when prescribing dopamine antagonists.

- e) A 23 year old male is admitted to the hospital with sudden onset of nausea and vomiting. Review of his medical records reveals that this patient has been admitted multiple times in the past with similar complaints. He has had an extensive evaluation for the cause of his symptoms and was diagnosed with “cyclic vomiting syndrome” during his previous admission.

Answer:

Supportive care and possible tricyclic antidepressants in adults