

Nausea: Diagnosis and Management



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Acknowledgement



This course was developed in 2004 with many revisions since then; Drs. Drew Rosielle and Kathryn Neuendorf were important contributors to past editions.

Disclaimer



While this program provides educational information, this information is not medical advice. Health care providers should exercise their own independent clinical judgment. Some of the information cites the use of a product in a dosage, for an indication, or in a manner other than that recommended in the product labeling.

Accordingly, the official prescribing information should be consulted before any such product is used.

Objectives



- Describe key questions to ask in the assessment of nausea.
- Identify five pathways of afferent input to the CNS vomiting center.
- List drugs from five different categories that can be effective for nausea/vomiting.

Case Question



- A 46 year old female with breast cancer metastatic to the bone has experienced with new onset nausea. She is vomiting at least 5 times a day and is unable to tolerate food due to the nausea. Prochlorperazine and ondansetron have been ineffective to control her nausea.
- What are key steps in the assessment of this patient's nausea?
- What are next step pharmacological options?

Nausea



- The term nausea means different things to different people; a thorough assessment is the key to distinguishing different etiologies;
- Key questions to ask include:



Assessment



1. Sensation of vertigo? → Vestibular irritation
2. Abdominal pain/ache? → GERD/Ulcer
3. Early satiety or anorexia? → Compressed stomach
or liver metastases
4. Headache w/ early morning nausea? → Brain Tumor
5. Positional vomiting or vomiting with no nausea → Reflux

Mechanism of Vomiting



- The reflex of vomiting is controlled by the:
 - **Vomiting Center**—control center in medulla for coordinating the efferent output of the vomiting motor sequence (vomiting reflex).
 - Sources of afferent input to the Vomiting Center which trigger the vomiting reflex, include:



Vomiting- Mechanisms



1. **Chemoreceptor trigger zone (CTZ)**—entry point for emetogenic blood or CSF–borne substances (morphine, chemotherapeutic agents, uremia); located in the area postrema outside the Blood Brain Barrier
2. **Cerebral cortex**—limbic system (e.g. anxiety-- anticipatory nausea)
3. **Visceral afferents** via vagus nerve—pharynx (gag), GI tract (gastric distension)
4. **Midbrain ICP receptors**—e.g. raised intracranial pressure
5. **Vestibular**—e.g. drugs: morphine, infections

Common causes of nausea



■ Gastrointestinal Causes

- obstruction
- gastritis, GERD
- gastric stasis, squashed stomach syndrome
- GI infection
- constipation
- abdominal carcinomatosis, extensive liver metastases
- acute effect of abdominal radiation and some chemotherapy agents

Other causes



- CNS—elevated ICP, posterior fossa tumors/bleed, infectious or neoplastic meningitis
- Drugs—opioids, chemotherapy, antibiotics
- Metabolic—hypercalcemia, liver failure, renal failure (uremia), sepsis
- Psychological—anxiety, pain, conditioned response (e.g. anticipatory nausea/vomiting).

Treatment



- **Non-Drug Therapy**
 - Behavioral treatments—relaxation, imagery, music, distraction, games
 - GI drainage for obstruction
 - NG placement or venting gastrostomy for obstruction
 - Fluid management—a patient with obstruction may benefit from reduction in parenteral fluids to decrease GI secretions and thus limit distention

Treatment



- Drug Therapy—General Principles
 - Try to match the cause of nausea with the most appropriate drug class
 - Start with low cost, low toxicity drugs
 - A trial and error approach is often needed
 - Treatment approaches should match severity of nausea
 - If nausea is constant, patient should have scheduled anti-emetic with PRN available for breakthrough nausea

Treatment



- Anti-emetics work via inhibition of one or more neurotransmitters active in the vomiting reflex, such as:
 - Acetylcholine
 - Dopamine
 - Histamine
 - Serotonin
 - Substance P

Matching cause to drug class



Stimulation of CTZ (drugs, uremia)	→	Dopamine or Serotonin antagonist
Movement-related nausea	→	Antihistamine
Anxiety	→	Benzodiazepine
Elevated intracranial pressure	→	Glucocorticoid
Gastric stasis	→	Metoclopramide
Constipation	→	Laxative
GERD	→	PPI

Anti-emetic examples



- **Scopolamine**: a very potent, pure anticholinergic agent.
- **Promethazine** (Phenergan ®): antihistamine with potent anticholinergic properties, very weak antidopaminergic agent. (Poor choice for opioid related nausea.)
- **Prochlorperazine** (Compazine ®): Potent antidopaminergic, weak antihistamine, anticholinergic agent.
- **Haloperidol**: Very potent anti-dopaminergic agent.
- **Lorazepam**: weak anti-emetic, little evidence of anti-emetic activity except in anxiety.

Common Agents by Drug Class



- **Dopamine antagonists**
 - Compazine ®, Thorazine ®, Haldol™, Inapsine ®, Zyprexa®
- **Serotonin antagonists**
 - Zofran ®, Kytril ®, Anzemet ®
- **Anti-Histamines / Anti-Cholinergic**
 - Benadryl ®, Vistaril ® , scopolamine, Phenergan ®

Other agents



- Pro-Motility Drug
 - Metoclopramide (Reglan ®)
- Cannabinoid
 - Marinol ®
- Glucocorticoid
 - prednisone
- Substance P receptor antagonist
 - Aprepitant (Emend ®): approved only for chemo-related nausea—no proven efficacy otherwise

Drugs for Continuous Infusion



- A continuous infusion of Thorazine ® or Reglan ® may be helpful in refractory N/V.
 - Either drug is started at 1.0 mg/hr and titrated upwards as needed.

What about Marijuana?



- THC in pill form (Marinol ®); indicated for chemotherapy related N/V.
- Typically a third-fourth line drug
 - Not very potent
 - Patients need to get “high”
 - Toxicity unacceptable to many patients, especially the elderly (dysphoria)
- Users claim that smoked marijuana is more effective than pills.

Opioid Induced Nausea



- Codeine and morphine seem to be the most emetogenic opioids
- Tolerance develops within 7 days for most patients.
- Nausea can be mediated by one of two mechanisms.
 - CTZ stimulation
 - Vestibular stimulation (patients report vertigo)
- No clear “best agent”
 - Compazine ® and/or scopolamine are good first agents; can also be used as prophylaxis.

Case Question



- A 46 year old female with breast cancer metastatic to the bone has been dealing with new onset nausea. She is vomiting at least 5 times a day and is unable to tolerate food due to the nausea. Prochlorperazine and ondansetron have been ineffective to control her nausea.
- What are key steps in the assessment of this patient's nausea?
- What are next step pharmacological options?

Answer



- Ask questions to help determine the cause
 - Medications?: New chemotherapy? Pain medications?
 - Constipation?
 - Spread of cancer to GI tract? To brain?
 - Anxiety induced?
- Since nausea is constant, anti-emetics should be scheduled for this patient in addition to being PRN
- Check if prior anti-emetics were prescribed in correct dose and how patient used them
- New anti-emetics can be selected based on cause or trial/error basis.

Learning Points



List 3 new things you learned from this presentation.

- 1.
- 2.
- 3.

References



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