Management of Constipation,Nausea and Anorexia in life-threatening illness

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Constipation

Etiology

- Constipation is reported in up to 70–100% of patients requiring palliative care.
- hypercalcemia,use of opioids ,anticholinergic effects of tricyclic antidepressants, inactivity and poor diets common among seriously ill patients
- can cause substantial pain and vomiting and also is associated with confusion and delirium
- Whenever opioids are used, preemptive treatment for constipation should be instituted.

Constipation

ASSESSMENT

- The Bowel Function Index can be used to quantify opioid-induced constipation
- patient’s previous bowel habits, any changes in subjective and objective qualities such as bloating or decreased frequency.
- Abdominal and rectal examinations should be performed to exclude impaction or an acute abdomen
- Radiographic assessments beyond a simple flat plate of the abdomen in cases in which obstruction is suspected are rarely necessary

Constipation

INTERVENTION

- physical activity, adequate hydration, and dietary treatments with fiber can be helpful
- fiber may exacerbate problems in the setting of dehydration or if impaired motility is the etiology.
- Fiber is contraindicated in the presence of opioid use.
- Stimulant and osmotic laxatives, stool softeners, fluids, and enemas are the mainstays of therapy

Constipation

INTERVENTION

- To prevent constipation from opioids and other medications, a combination of a laxative and a stool softener (such as senna and docusate) should be used.
- If after several days of treatment a bowel movement has not occurred, a rectal examination to remove impacted stool and place a suppository is necessary.
- For patients with impending bowel obstruction or gastric stasis, octreotide to reduce secretions can be helpful.
- For patients in whom the suspected mechanism is dysmotility, metoclopramide can be helpful.

TABLE 9-5 Medications for the Management of Constipation

INTERVENTION	DOSE	COMMENT
Stimulant laxatives		These agents directly stimulate peristalsis and may reduce colonic absorption of water.
Prune juice	120–240 mL/d	Work in 6–12 h.
Senna (Senokot)	2–8 tablets PO bid	
Bisacodyl	5–15 mg/d PO, PR	
Osmotic laxatives		These agents are not absorbed. They attract and retain water in the gastrointestinal tract.
Lactulose	15–30 mL PO q4–8h	Lactulose may cause flatulence and bloating.
Magnesium hydroxide (Milk of Magnesia)	15–30 mL/d PO	Lactulose works in 1 day, magnesium products in 6 h.
Magnesium citrate	125–250 mL/d PO	
Stool softeners		These agents work by increasing water secretion and as detergents, increasing water penetration into the stool.
Sodium docusate (Colace)	300–600 mg/d PO	Work in 1–3 days.
Calcium docusate	300–600 mg/d PO	
Suppositories and enemas		
Bisacodyl	10–15 PR qd	
Sodium phosphate enema	PR qd	Fixed dose, 4.5 oz, Fleet's.

Nausea

- Among patients with cancer, chemotherapy and RT are common causes of nausea and vomiting
- Despite adherence to published guidelines, breakthrough nausea and vomiting affects up to 40 percent of patients treated with either modality.
- Chronic nausea is also a significant problem in patients with terminal cancer who are not receiving active cancer treatment and in other palliative care populations with CKD and HF.

Nausea

- Nausea and vomiting are both caused by stimulation at one of four sites: the GI tract, the vestibular system, the chemoreceptor trigger zone (CTZ), and the cerebral cortex.
- Medical treatments for nausea are aimed at receptors at each of these sites:
- GI tract contains mechanoreceptors, chemoreceptors, and (5-HT3) receptors
- vestibular system probably contains histamine and acetylcholine receptors
- CTZ contains chemoreceptors, dopamine type 2 receptors, and 5-HT3 receptors
- nausea that most likely is mediated by the cortex is anticipatory nausea before a dose of chemotherapy or other noxious stimuli.

Nausea

Specific causes

- metabolic changes (liver failure, uremia from renal failure, hypercalcemia), bowel obstruction,
- constipation,
- infection,
- GERD,
- vestibular disease,
- brain metastases,
- medications (including antibiotics, NSAIDs, proton pump inhibitors, opioids, and chemotherapy),
- radiation therapy
- Anxiety

Nausea

Interventions

- Medical treatment of nausea is directed at the anatomic and receptor-mediated cause revealed by a careful history and physical examination.
- When no specific cause of nausea is identified, many advocate beginning treatment with either metoclopramide,
- a 5-HT3 receptor antagonist like ondansetron, granisetron or
- a dopamine antagonist such as chlorpromazine, haloperidol or prochlorperazine.

Nausea

Interventions

- When decreased motility is suspected, metoclopramide an effective treatment
- inflammation of the GI tract is suspected, glucocorticoids, such as dexamethasone.
- For nausea that follows chemotherapy and radiation therapy, one of the 5-HT3 receptor antagonists or neurokinin-1 antagonists, such as aprepitant or fosaprepitant, is recommended
- When a vestibular cause (such as “motion sickness” or labyrinthitis) is suspected, antihistamines, such as meclizine (whose primary side effect is drowsiness), or anticholinergics, such as scopolamine, can be effective.

Nausea

Interventions

- In anticipatory nausea, patients can benefit from non-pharmacological interventions, such as biofeedback and hypnosis. The most common pharmacological intervention for anticipatory nausea is a benzodiazepine, such as lorazepam
- Clinicians should attempt prevention of postchemotherapy nausea, rather than simply providing treatment after the fact.

Nausea

Interventions

- Guidelines for prevention of CINV are based upon emetic risk category .
- For patients with breakthrough CINV, ensure that the patient is receiving the antiemetic appropriate for the drug(s) being given and the correct dose
- If poor emesis control is documented with an appropriate antiemetic regimen, the regimen should be adjusted to one typically used for a higher risk group.
- For patients who are unable to take oral medications, metoclopramide, dexamethasone, and haloperidol have been safely administered intravenously and subcutaneously.

Interventions

- Breakthrough symptoms can be managed by:
- By adding agents such as lorazepam or alprazolam, olanzapine, or a dopaminergic antagonist (eg, prochlorperazine, thiethylperazine, haloperidol),
- By substituting high-dose intravenous (IV) metoclopramide (30 to 40 mg/day, titrating as needed to no more than 60 to 100 mg/day) for the 5-HT3 receptor antagonist,
- By switching to a different 5-HT3 receptor antagonist, given incomplete cross-resistance between agents

Nausea

- The risk for radiotherapy-induced nausea and vomiting (RINV) is stratified into four categories depending on radiation field
- Specific recommendations for prophylaxis based upon these risk categories are available
- unable to take oral medications, metoclopramide, dexamethasone, and haloperidol have been safely administered intravenously and subcutaneously

Nausea

Non-cancer conditions

- For patients with uremia-induced nausea, **prokinetic** agents،**haloperidol** or **ondansetron** are potentially useful agents.
- For patients with end-stage liver disease, nausea may be due to gastroparesis, increased abdominal pressure, or centrally mediated by circulating toxins and bilirubin
- For severe hepatic impairment (Child-Pugh C cirrhosis), doses of ondansetron should be limited to no more than 8 mg/24 hours, and metoclopramide should be limited to no more than 60 mg/24 hours

Anorexia and cachexia

- Anorexia :loss of appetite or reduced caloric intake
- Cachexia : multifactorial syndrome ,continuous loss of skeletal muscle mass, with or without loss of fat mass, that cannot be fully reversed by conventional nutritional support
- high prevalence of anorexia-cachexia syndrome in patients with advanced cancer, but it also can occur in the setting of other chronic illnesses including advanced HIV/AIDS, heart failure, CKD, COPD.

Anorexia and cachexia

- Contributory factors include chronic fatigue or nausea, altered taste, depression, pain, xerostomia, disorders of gastrointestinal motility, constipation, medications, and aging

- cytokines as metabolic derangements associated with the hypermetabolic state that characterizes cancer-bearing states, and the inflammatory response may play a unifying central role

- Chemotherapy can also contribute to muscle wasting, and chronic opioid use can result in hypogonadism and subsequent loss of lean body mass

Anorexia and cachexia

- All palliative care patients should be screened for nutritional status and weight loss.
- careful history is focused on nutritional issues, including risk factors that compromise the ability to obtain or take in nutrition,
- PH/E: focusing on loss of subcutaneous fat, muscle wasting (temporal region, deltoids, and quadriceps with loss of bulk and tone by palpation), edema (sacral or ankle), or ascites.
- most commonly used objective measures of nutritional status are serial measurement of body weight and observations of dietary intake

Anorexia and cachexia

- screen all cancer patients with weight loss for thyroid abnormalities, which are more common in patients treated with tyrosine kinase inhibitors
- We also screen for adrenal insufficiency in cancer patients who have bilateral adrenal metastasis or in those with a clinical suspicion for adrenal insufficiency
- For most hypogonadal men, the benefits of testosterone replacement are unclear

Anorexia and cachexia

Interventions

- able to eat should be recommended to have small, frequent meals that are dense in calories
- some patients may benefit from nutritional supplementation
- patients and families should be counseled that increasing caloric intake does not reverse the underlying process and that anorexia and cachexia are not uncommon symptoms but a natural process that occurs at the end of life.

Anorexia and cachexia

- persistent anorexia: pharmacologic treatments stimulate appetite, they will not reverse cachexia
- anorexia related to cancer, HIV/AIDS, or other underlying pathology (but notESKD), suggest a short trial of **megestrol acetate**
- risk of edema, the risk of thromboembolic phenomena, and an increased risk of death
- a two-week trial of megestrol to assess for improvement in appetite may be considered, and if ineffective, discontinued
- To minimize adverse effects, it is recommended to start at the lowest effective dose (starting at 160 mg/day) and titrate to a maximum of 800 mg/day
- **Glucocorticoids** stimulate appetite;
- all of the data are in cancer patients with anorexia-cachexia syndrome, and there is no evidence for the use of these agents in anorexia due to end-stage nonmalignant conditions

Anorexia and cachexia

Treatments needing further study

- Cannabis and cannabinoids
- Omega-3 fatty acids/EPA and DHA
- Amino acids/carnitine supplements
- NSAIDs/COX-2 selective inhibitors
- Olanzapine
- Growth hormone and ghrelin