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Managing Common Gastrointestinal Symptoms at the End of Life

❖ Karl E. Miller, MD; Marti Miller, RN, CRNH

❖ After pain control, gastrointestinal symptoms are among the more common problems that healthcare professionals face when providing care at the end of life. These can range from mild and annoying to severe symptoms requiring emergency interventions. These symptoms include nausea and vomiting, dyspepsia and gastroesophageal reflux disease, constipation, hepatic failure, anorexia, and intractable hiccups. Treatment of these various gastrointestinal symptoms includes nonpharmacological and pharmacological management strategies.

Karl E. Miller, MD, *is Medical Director of Adventa Hospice, Chattanooga, Tenn, and an associate professor in the Department of Family Medicine, University of Tennessee College of Medicine, Chattanooga Unit, Chattanooga, Tenn.*

Marti Miller, RN, CRNH, *is the administrator for Adventa Hospice, Chattanooga, Tenn. She is a Certified Registered Nurse for Hospice.*

K E Y W O R D S

antiemetics
constipation
hepatic failure
dyspepsia
gastroesophageal reflux disease

Second to pain control, gastrointestinal symptoms are one of the more common problems that healthcare professionals face when providing care at the end of life. These can range from mild and annoying to severe symptoms requiring emergency interventions. To treat these symptoms, individuals involved with the care of these patients must have a treatment plan based on a thorough assessment and an understanding of the underlying pathology. The following symptoms are reviewed: nausea and vomiting, dyspepsia and gastroesophageal reflux disease (GERD), constipation, hepatic-related symptoms and intractable hiccups.

❖ NAUSEA AND VOMITING

There are many causes of nausea and vomiting in the terminally ill patient. Gastrointestinal causes include constipation, poor gastric emptying, bowel obstruction, oral and/or esophageal infections, liver failure, ascites, and extrinsic pressure on the stomach. Gastrointestinal side effects from medications also need to be considered. Other possible causes include side effects of radiation or chemotherapy, increased intracranial pressure, uremia, hypercalcemia, vestibular disturbances, cough, anxiety, and disease progression.

The initial assessment of a patient with nausea and vomiting includes a history and examination. The history should include questions about the pattern of the symptoms:

- Does it occur before or after meals?
- Are there any precipitating factors?
- Are there any heartburn or reflux symptoms?
- Has there been any change in bowel habits?

In addition, information concerning pain related to the nausea and vomiting can help delineate if these symptoms are secondary to specific disease processes. An assessment of dietary habits also is important. In some cases, nausea and vomiting can be related to force-feeding or overfeeding patients. This assessment should include information regarding fluid status because dehydration can sometimes lead to nausea and vomiting. A past history of peptic ulcer disease, chemotherapy or radiation therapy to the abdomen, or metastatic or primary brain tumor, as well as food intolerances should be explored with patients. It is important to review all of the patient's current medications, including over-the-counter medications and alternative therapies. Many medications have significant gastrointestinal side effects and can cause nausea. Some of the more common medications include opioids, nonsteroidal anti-inflammatory drugs including aspirin, some antibiotics, estrogen, digoxin, selective serotonin reuptake inhibitors, potassium, and cytotoxins.[1]

The assessment of patients with nausea and vomiting includes a focused physical examination, which also involves an oral examination evaluating for candidiasis or other oral lesions that may make swallowing difficult. Oral assessments involve the entire oral cavity, tongue, gingiva, mucous membranes, and lips. Hygiene issues should be addressed with the patient to explore any underlying causes. Nutritional and fluid intake assessment is equally important because underlying issues relative to force feedings can be identified at this time. Skin assessment also can provide information about fluid and nutritional status. Decreased skin turgor may indicate dehydration but it also may indicate malnutrition. The abdominal examination starts with observation to determine if there are any signs of distension or cachexia. The next step is auscultation for bowel sounds including the tone and character. High-pitched or hyperactive bowel sounds may indicate a partial or total obstruction, whereas absent bowel sounds may indicate an ileus. Palpation of the abdomen includes observing for any areas of tenderness and masses. A rectal examination may be indicated if constipation or impaction is suspected as a possible etiology of these symptoms. This can help determine what would be the best management strategy for patients.

If possible, the treatment for nausea or vomiting should start with reversing the underlying cause[2] (Figures 1 and 2). However, it is important to determine the exact etiology prior to initiating treatment. Prokinetic agents may improve symptoms in patients with delayed gastric emptying but will exacerbate the symptoms in the case of bowel obstruction.

Dietary modifications can be initiated before the onset of nausea and vomiting or included in the treatment plan after these symptoms have developed (Figure 3). Minor dietary manipulations may reduce the likelihood of developing these symptoms and could potentially reduce the need for medications. These include small, frequent meals, avoiding fasting periods, and taking sips of fluids on a regular basis.

Various medications are available to treat nausea and vomiting in terminally ill patients[2] (Figure 4). These agents act on various sites including the chemoreceptor trigger zone, the vomiting center in the medulla, serotonin receptors, and gastrointestinal smooth muscles.

Haloperidol (Haldol, Ortho McNeil, Raritan, NJ) is one of the more commonly used agents for treating nausea and vomiting in terminally ill patients who do not respond to first-line agents. This medication controls these symptoms by acting on the chemoreceptor trigger zone.[2] Haloperidol comes in multiple forms including tablets, injectable liquid, compounded topical gels, rectal suppositories, and as a sublingual, bland-tasting concentrated liquid (2 mg/mL). The advantages of haloperidol over some of the other agents are that at the lower doses used to treat nausea and vomiting it has less sedating and anticholenergic side effects. In addition it has minimal cardiac and central nervous side effects.

Phenothiazines are another group of medications that can treat nausea and vomiting. These agents work on the chemoreceptor trigger zone. These medications are available in oral and rectal preparations, and compounded topical gels. The disadvantages of these agents are that they can sedate patients, have anticholenergic side effects, and they tend to be short-acting.

Corticosteroids can be used to control nausea and vomiting. Some authors suggest that these should be used as first-line agents in treating these symptoms at the end of life.[3] The disadvantage to medications in this class is that they can increase the risk for dyspepsia, ulcers, gastritis, and upper gastrointestinal bleeding.

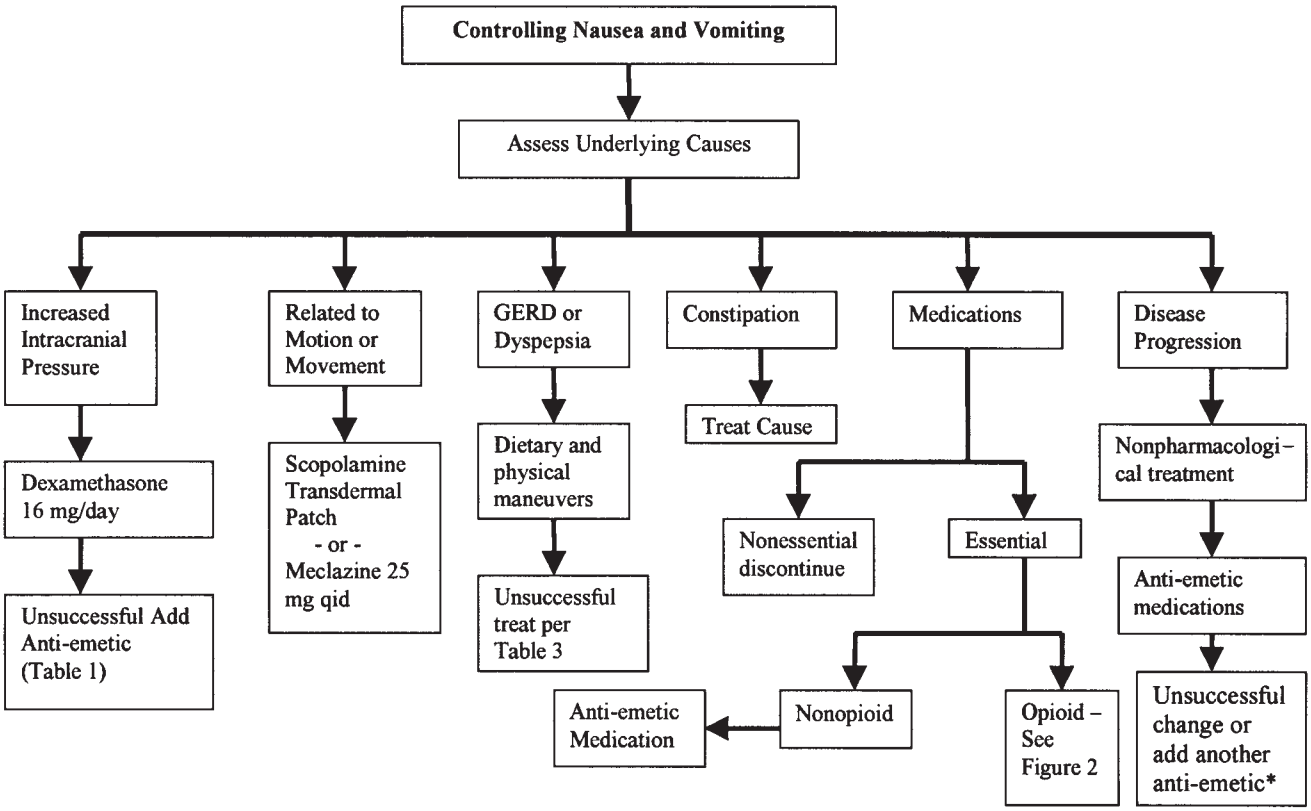

Figure 1. Controlling nausea and vomiting.

There is currently only one prokinetic agent available, metoclopramide (Reglan). This medication works by accelerating forward peristalsis in the gastrointestinal tract and increasing the tone of the gastroesophageal junction. Metoclopramide can be used in any patients who have nausea or vomiting.[4] This medication should be given 30 minutes before meals and at bedtime. Metoclopramide has the advantage of being relatively inexpensive and is available for subcutaneous pumps. The disadvantage of metoclopramide is that it has central nervous system side effects including restlessness, nervousness, extrapyramidal effects, and tardive dyskinesia. Metoclopramide and haloperidol should never be used in combination because together they are likely to cause dystonia and stiffness.[1]

Antihistamine agents can be used to treat nausea and vomiting. These agents act directly on the vomiting center in the medulla. Sedation is the major side effect of these medications and can limit their usefulness. These medications are available over-the-counter and are relatively inexpensive.

There are four agents that should be reserved for resistant or intractable nausea and vomiting. Three of these medications are selective 5-HT3 receptor antagonists and include dolasetron (Anzmet, Aventis, Kansas City, Mo), ondansetron (Zofran, Glaxo Smith Kline, Research Triangle Park, NC), and granisetron (Kytril, Roche Laboratories, Nutley, NJ). All three are available in parenteral and oral forms. In one recent study, both ondanestron and granisetron have been found to be equally effective, so the agent selection can be based on cost of medication.[5] Disadvantages to these medications include the potential for tachyphylaxis (developing tolerance to medications, thus requiring higher doses to control symptoms) and expense. Dronabinol (Marinol, Unimed Pharmaceuticals, Deerfield, Ill), the active compound in marijuana, is another agent available for resistant or intractable nausea and vomiting. This agent has significant side effects including somnolence, hallucinations, and mental dullness. It is also expensive.

There are products that can be combined and used successfully in patients who do not respond to the first- or

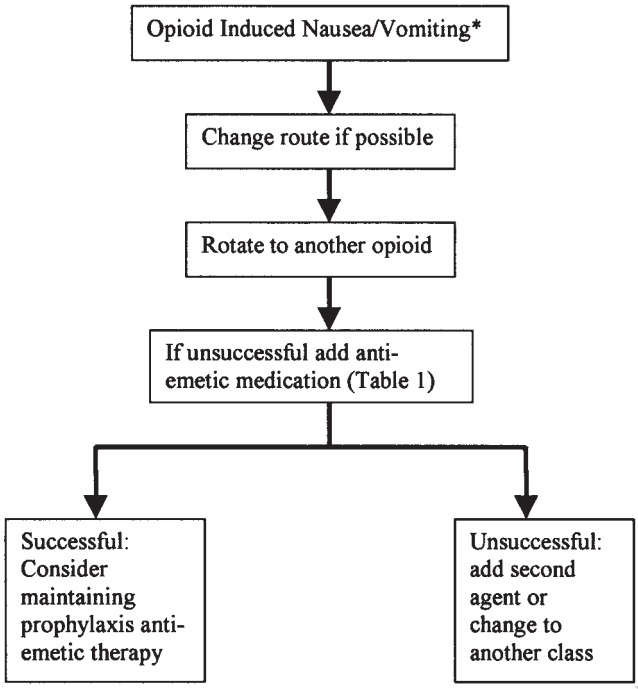

Figure 2. Controlling opioid-induced nausea/vomiting.

second-line agents. One such combination is known as ABHD: lorazepam (Ativan, Wyeth Laboratories, Philadelphia, Pa), diphenhydramine (Benadryl, Pfizer, Inc., Morris Plains, NJ), haloperidol (Haldol), and dexamethasone (Decadron, Merck and Co., West Point, Pa). These products can be tailored to the individual patients symptoms, with specific drugs added or omitted.

❖ DYSPEPSIA/GERD

Other common gastrointestinal symptoms experienced by patients at the end of life include dyspepsia and GERD. These symptoms can range from annoying pain and discomfort to severe chest pain. Treatment for these symptoms includes nonpharmacological and pharmacological strategies.

Nonpharmacological management includes physical measures and dietary modifications. The physical measures include maintaining an upright position during a meal and for 45 to 60 minutes after eating, avoiding eating within 2 hours of bedtime, avoiding tight-fitting clothing around the abdomen, and elevating the head of the bed 6 inches when sleeping. If the patient is a smoker, stopping smoking can also alleviate symptoms. Dietary modifications include avoiding caffeine, chocolate, alcohol, mint, carbonated beverages, citrus juices, tomato products, decaffeinated coffee and foods that have high fat content. These foods tend to irritate the gastrointestinal tract and decrease the lower esophageal sphincter pressures, thus increasing dyspepsia and GERD symptoms. In addition, eating small quantities of problem foods can reduce these symptoms in patients who prefer not to give up their favorite foods.

Pharmacological options for the treatment of dyspepsia and GERD include four classes of medications: antacids, histamine H_2-receptor antagonists (also known as H_2 blockers), proton pump inhibitors, and a prokinetic agent (Table 1). Antacids are available over the counter, can be used to treat patients with mild symptoms, and are inexpensive. The disadvantage of antacids is that routine use can interfere with the absorption of other oral medications.

The advantages of the H_2 blockers are that they tend to be well tolerated and some are available in a less expensive generic form. They can cause side effects such as dizziness, central nervous system disturbances, and gastrointestinal symptoms. Cimetadine (Tagamet, Glaxo Smith Kline, Research Triangle Park, NC) should be avoided because it has a significant side effect profile including mental confusion, gynecomastia, blood dyscrasia, headaches and arthralgia. In addition, cimetadine has multiple drug-drug interactions.

Second-line therapy in patients with dyspepsia or GERD that do not respond to the H_2 blockers include proton pump inhibitors. These medications are well tolerated and patients have tended to respond well. The only drug-drug interaction that these medications have is that they can interfere with the absorption of pH-sensitive medications (eg, ketaconazole, iron, digoxin, etc.). Conventional therapy to dyspepsia and GERD has been to start with H_2 blocker therapy and if symptoms do not resolve in 2 to 4 weeks, patients should be switched to a proton pump inhibitor.[6]

Another second-line option is to add metoclopramide, a prokinetic agent, to either H_2 blocker or proton pump inhibitor therapy. This medication increases the lower esophageal sphincter pressure and improves gastric emptying. Possible side effects related to this medication include restlessness, drowsiness, fatigue, extrapyramidal effects, tardive dyskinesia, and dizziness.

❖ CONSTIPATION

Constipation is one of the most common complaints of patients at the end of life. Various causes of constipation

1. Sip fluids at frequent intervals separate from eating solids
2. Discourage fasting
3. Small frequent meals and snacks
4. Cold or room temperature foods may be better tolerated
5. Avoid high-fat, high-fiber, spicy or gas producing foods
6. Discourage the use of alcohol
7. Avoid meal preparation, smells may worsen symptoms
8. Limit foods with strong odors
9. Advise against lying down immediately after meals if possible

Figure 3. Dietary instructions to reduce or control nausea and vomiting.

include inactivity, dehydration, low-fiber diet, gastrointestinal motility disorders, and reduced defecation secondary to weakness and medication side effects. Constipation can be present even if patients continue to have bowel movements; some patients have diarrhea or loose stools resulting from overflow leakage around fecal impaction.

An assessment for constipation needs to be performed on the first day patients present to the healthcare team and continue on subsequent visits. This includes asking the time of last bowel movement, was it normal, texture of the stool (hard, soft, loose, etc.) and quantity of stool. Information about any pain pattern before, during, or after bowel movements as well as other gastrointestinal complaints also should be explored. An important piece of the evaluation includes any prior history of reliance on bowel preparations. Previous reliance on bowel preparations may result in an increased dosing requirement of bowel treatment medications. A review of current medications including over-the-counter preparations and any alternative therapies should be completed.

The physical examination of the abdomen needs to completed in the same manner as described previously. Consistent with constipation, a mass may be palpated in the left lower quadrant suggesting stool in the descending or rectosigmoid colon. The abdomen can be tender to palpation in patients with constipation and a rectal examination may reveal hard, impacted stool. If the rec-

TABLE 1
Treatment Medications for Dyspepsia/GERD

	Dyspepsia Dose	GERD Dose
H_2 Blockers		
Cimetidine (Tagamet)	800 mg @hs	800 mg bid
Famotidine (Pepcid)	20-40 mg daily	40 mg daily
Nizatidine (Axid)	150 mg bid	150 mg bid
Ranitidine (Zantac)	150 mg bid	150 mg bid
Proton Pump Inhibitors		
Esomeprazole (Nexium)	20 mg daily or bid	40 mg daily or bid
Lansoprazole(Prevacid)	15 mg daily	30 mg daily
Omeprazole (Prilosec)	20 mg daily	20-40 mg daily
Pantoprazole (Protonix)	40 mg daily	40 mg daily
Rabeprazole(Aciphex)	20 mg daily	20 mg daily

GERD, gastroesophageal reflux disease; bid, twice a day; hs, hour of sleep.

Chemoreceptor trigger zone

Butyrophenone

Haloperidol (Haldol) 0.5-1.0 mg PO, SL, or IM every 8-12 hours

Phenothiazines

Chlorpromazide (Thorazine) 25-50 mg PO or 50-100 mg rectally every 4-6 hours

Prochlorperazine (Compazine) 10 mg PO or 25 mg rectally every 4-6 hours

Promethazine (Phenergan) 25-50 mg PO or rectally every 4 hours

Thiethylperazine (Torecan) 10 mg PO or rectally every 8 hours

Prokinetic agent

Metoclopramide (Reglan) 10-30 mg PO qid

Vomiting center activity

Antihistamines

Chlortrimeton sustained release 12 mg PO every 12 hours

Diphenydramine (Benadryl) 25-50 mg PO every 4-6 hours

Serotonin blockade activity

Ondansetron (Zofran) 4-8 mg PO, IV, IM every 8 hours

Granisteron (Kytril) 1 mg PO, IV, IM every 12 hours

Dolasetron (Anzemet) 50-100 mg PO, IV, IM

Other agents

Dronabinol (Marinol) 5-10 mg PO every 4-6 hours

Prednisone 20 mg PO qid

Dexamethosone 2-10 mg PO or IM every 12 hours

Figure 4. Medications used for nausea and vomiting. PO, by mouth; SL, sublingual; IM, intramuscular; qid, four times daily; IV, intravenous.

tum is empty of stool, the impaction could be present higher in the colon.

The first intervention for patients is to prevent constipation from becoming a problem. In addition to becoming less active, many patients at the end of their lives are on medications that can cause constipation, particularly opioids. When starting an opioid or observing a patient who is declining, proactive steps must be taken to reduce the likelihood patients will develop constipation. Bowel preparations need to be initiated at the same time opioids are started to prevent this unnecessary side effect. Adding both a stool softener and laxative to their medication regimen and titrating until the patient is having regular bowel movements can prevent constipation, therefore reducing the likelihood of this unpleasant symptom. Patients taking opioids will require significantly higher doses of laxatives to prevent constipation than those who are not taking opioids for pain control.[7]

Initial therapeutic interventions include mobilizing the patient, encouraging intake of fluids and dietary roughage, eliminate constipating medications, adding bulking agents, and checking for impaction. In most terminally ill patients these interventions are not feasible because they can cause more problems than they will solve. Instead, laxatives or stool softeners should be given, using a product that the patient prefers (Figure 5). The best regimen uses both bowel stimulants and stool softeners.[8,9] If a patient suffers significant cramping with the combination medication, it can be relieved by eliminating the bowel stimulant.[8,9] Milk of

Stool softeners

- Lubricants - Mineral oils
- Docusate - DSS, Colace, Surfak

Stimulants

- Magnesium compounds
  - Magnesium citrate
  - Milk of magnesia
- Lactulose
  - Polyphenolics
  - Ex-Lax
  - Dulcolax
- Anthracenes
  - Senna (Senokot, Ex-prep)
  - Danthron (Doxidan, Dorbane)
  - Casanthranol (Peri-colase)
- Combination softener/laxative
  - Senokot-S

Figure 5. Treatment medications for constipation.

magnesia, cascara, bisacodyl (Dulcolax), or 8 ounces of magnesia citrate can be used in patients who do not respond to the first-line agent. Another option that has been proven to be effective in treating fecal impaction and constipation is 1 L of polyethylene glycol/electrolyte solution daily for 3 days.[10] The disadvantage to this treatment option is the amount of fluid intake required to be effective.

❖ HEPATIC SYMPTOMS

There are multiple causes of hepatic symptoms in patients at the end of their lives. Some patients have primary liver disease that progresses into the terminal phase. Others have primary or metastatic cancer that results in the progression of liver disease. Three of the more common problems that healthcare workers face in these patients include ascites, pruritis, and hepatic encephalopathy.

Ascites is the accumulation of fluid in the abdomen usually as a result of hepatic cirrhosis. The patient's symptoms can include abdominal distension, early satiety, constipation, and, in severe cases, respiratory symptoms. Examining the abdomen for a fluid wave and shifting dullness to percussion can confirm the diagnosis.

Sodium restriction (40-60 mEq/day) is the initial treatment for the patients with ascites. Of course, this must be balanced with dietary wishes, especially in patients with significant loss of appetite. In addition to dietary management, the treatment for ascites is diuretic therapy. The first-line agent is spironolactone 100 mg/day initially and titrated up to 400 mg/day.[11] Furosemide also can be used as a treatment option but this diuretic tends to have a higher incidence of diuretic-induced azotemia than spironolactone. In addition, furosemide can cause more electrolyte abnormalities. Severe cases of ascites or those that do not respond to single diuretic therapy may benefit from combining spironolactone and furosemide. Patients who do not respond to medical management may benefit from a paracentesis. This procedure does have limitations because it tends to only temporarily relieve symptoms with reaccumulation of fluid.

Pruritis can be related to obstruction of bile flow from the liver to the bowel, with the result that bile salts accumulate in the skin, causing patients to itch. Pruritis can start prior to any visible signs of jaundice. Treatment options include using antihistamines such as 25 to 50 mg of diphenhydramine (Benadryl) every 4 hours or 25 to 50 mg of hydroxyzine (Atarax, Pfizer, Inc., New York, NY) every 6 hours. A common side effect of this class of medication is sedation. If these medications do not control symptoms, a 10-mg tablet of methyltesterone buccal 3 times per day or 4 g of cholestyramine (Questran, Bristol-Myers Squibb, Princeton, NJ) every 8 hours are treatment options. High-dose corticosteroids may also be used to relieve biliary pressure.[1]

Hepatic encephalopathy is a neuropsychiatric syndrome that occurs as a result of advanced, decompensated liver disease. Mental status and motor changes occur as a result of this disease. Patients are classified into different stages of hepatic encephalopathy based on these changes (Table 2).[11] This encephalopathy can be precipitated by deterioration of hepatic function, medications, gastrointestinal hemorrhage, increased dietary protein, infection, and azotemia.

Treatment of patients with hepatic encephalopathy consists of dietary changes and medications. The dietary recommendation is to limit the protein intake to approximately 40 g/day but this needs to be balanced with the likelihood that many of these patients have low serum albumin and protein, which can be exacerbated with a low-protein diet.

Lactulose is effective in lowering serum toxins and reversing hepatic encephalopathy.[1] The usual dose is 30 to 45 mL orally every 2 hours until diarrhea develops.

TABLE 2
Stages of Hepatic Encephalopathy

Stage	Mental Status	Motor Changes
Subclinical	No changes on examination may have impaired work performance or driving	Impaired performance on figure drawing or number connection
I	Mild confusion, apathy, agitation, euphoria, anxiety, restlessness	Fine tremor, asterixis, slowed coordination
II	Drowsiness, disorientation inappropriate behavior, lethargy	Asterixis, primitive reflexes ataxia, paratonia
III	Somnolent but can be aroused; marked confusion, incomprehensible speech	Hyperreflexia, myoclonus, incontinence, hyperventilation
IV	Coma	May respond to painful stimuli initially but progress to no response, decerebrate posturing

Adapted from: Scharschmidt BF. Acute and chronic hepatic failure and hepatic encephalopathy. In: *Cecil Textbook of Medicine*. 20th ed. Bennett JC, Plum F ed. Philadelphia, Pa: WB Saunders; 1996:797-800.

If patients are unable to tolerate oral medications, this may be given by a retention enema. Maintenance therapy is based on the amount of medication needed to produce two to four soft stools per day.

❖ INTRACTABLE HICCUPS

Intractable hiccups are rare but can cause a significant amount of distress in both patients and families. Initial measures to treat these hiccups are aimed at vagal stimulation. This can be accomplished with pharyngeal stimulation by swallowing ice water or granulated sugar. Other non-pharmacological measures include using a rebreathing bag or mask and using a nasogastric tube to decompress the stomach.

If these measures fail, medications can be used to treat intractable hiccups. Ten to 20 mg of metoclopramide administered orally four times per day can be used to treat these hiccups. In some cases this is limited because patients cannot tolerate oral medications. In those patients thorazine 25 mg may be given by slow intravenous infusion. Three to 5 mg of haloperidol every 8 hours may also be effective in treating intractable hiccups. In severe cases, haloperidol may be given subcutaneously. Recent studies have found that baclofen and nifedipine are alternative treatment options for patients with intractable hiccups.[12]

❖ PSYCHOSOCIAL AND SPIRITUAL ISSUES

The complete assessment of patients with gastrointestinal symptoms at the end of life needs to include psychosocial and spiritual issues. When dealing with gastrointestinal symptoms, healthcare workers need to be aware of the potential impact that psychosocial and spiritual issues can have on these symptoms. Relying purely on medications to treat gastrointestinal symptoms may result in inadequate management of these symptoms. When psychosocial or spiritual issues are identified as impacting the gastrointestinal tract, appropriate referral to interdisciplinary team members can provide relief for these individuals.

❖ SUMMARY

When providing care for patients at the end of their lives, healthcare providers need to be aware of how to intervene and treat common gastrointestinal symptoms. These treatment strategies need to be based on an understanding of the underlying cause of the symptoms and include nonpharmacological and pharmacological management. By controlling gastrointestinal symptoms, patients' quality of life will benefit from these interventions.

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Address correspondence to Karl E. Miller, MD, Associate Professor, Department of Family Medicine, 1100 East Third Street, Chattanooga, TN 37403 (e-mail: millerkarle@hotmail.com).