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The Management of Nausea at the End of Life

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The evaluation and management of nausea in patients near the end of life can be more challenging than that of nausea in patients undergoing antineoplastic therapies. Unlike in the oncology setting in which nausea is primarily managed using antiemetic regimens that have been developed with the neuropharmacology and emetogenic potentials of chemotherapy agents in mind, many patients receiving end-of-life care have nausea of multifactorial etiology. Patients also may be older with reduced physiologic ability to metabolize and clear drugs. Therefore, typical antiemetics in regimens initially selected for oncology patients may be ineffective. In this article, the prevalence, manifestation, and pathophysiology of nausea experienced by patients near and at the end of life will be reviewed, with a focus on pharmacological and nonpharmacological interventions that have been found to effectively manage this symptom in this patient population.

KEY WORDS

end of life, management, nausea, palliative care, pharmacology

Nausea is defined as an "unpleasant sensory and emotional experience"[1(p88)] associated with the feeling of fullness in the epigastric and upper abdominal area, with or without a need to vomit.[1,2] Dry heaving or retching can also occur as a result of spasmodic contraction of the abdominal muscles against a closed glottis. Nausea with vomiting can be a protective reflex to rid the body of an offending agent.[2]

The management of nausea experienced by patients near and at the end of life can present more challenges than other populations. Unlike in the oncology setting where nausea is managed using antiemetic regimens that have been developed in accordance with the neuropharmacology and emetogenic potential of chemotherapy, patients at the end of life may experience nausea because of a multitude of factors. In addition, patients who are older may have a reduced physiologic ability to metabolize and clear drugs.[3] In these populations, the use of the typical antiemetics recommended in regimens for oncology patients may be ineffective.

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PREVALENCE OF NAUSEA

The prevalence of nausea and vomiting in the end-of-life population varies. As many as 50% to 60% of patients with advanced cancer experience nausea[2,4]; 50% of patients with heart and liver failure and 30% to 50% of patients with renal failure experience this symptom.[2] As many as 70% of patients may experience moderate to severe nausea in the final week of life.[3,5] The following increase this risk: female sex; younger age; history of low alcohol intake and anxiety; gynecological, stomach, and esophageal tumors; medications such as opioids; and fluid and electrolyte imbalances that can occur from dehydration and malnutrition.[2,3,6] Near the end of life, nausea can be chronic or occur intermittently with variable severity[3]; because of its unpredictable trajectory, nausea may be inadequately assessed and managed.[7]

ETIOLOGY AND MANIFESTATIONS OF NAUSEA

Patients can describe nausea as queasiness or an upset stomach and may experience tachycardia, pallor, cold sweat, and diarrhea, which are typical symptoms that arise from a decreased parasympathetic and an increased sympathetic stimulation of the autonomic nervous system.[1,3,4] Near the end of life, nausea may be experienced within a symptom cluster that includes constipation, appetite loss, bloating, and weight loss.[4] Nongastrointestinal (non-GI) symptoms such as fatigue, dyspnea, and drowsiness also occur.[3] Nausea may also be associated with changes in emotion and cognition, as supported by functional magnetic resonance imaging studies.[8] In these patients, nausea may be due to a number of disease processes and/or the direct result of medications, as noted hereinafter.

Bowel Dysfunction Associated With Nausea

Bowel dysfunction is a common cause of nausea in the end-of-life population, the prevalence and severity of which increase toward the end of life.[6] Gastroparesis is common,[3] resulting from GI malignancies, neuropathy from Parkinson disease, and/or opioid therapy.[3,9] Gastroparesis can lead to constipation and functional bowel obstruction, which can also cause nausea,[3] and patients often report intermittent

nausea that is associated with bloating and relieved by vomiting.[3,5] The clustering of nausea with early satiety and epigastric pain may indicate GI irritation and cancer-associated functional dyspepsia syndrome.[3] Other less common GI causes of nausea include ulcers, ascites, hepatitis, and adhesions.[2,3]

Medications Implicated in Nausea

In 30% to 40% of patients who are nearing the end of life, nausea is persistent and not relieved by vomiting.[3] In these patients, nausea may be secondary to the effects of medications including opioids, antibiotics, anticonvulsants, and nonsteroidal anti-inflammatory agents on intracranial receptors.[2,5] Opioid use among those at the end of life, specifically those receiving hospice benefits, is estimated at 88% to 94%[10]; nausea tends to be higher in opioid-naive patients and improves with continued therapy, but it can persist in some. The abrupt withdrawal of corticosteroids, commonly used as an adjunct for pain and edema, can also lead to adrenal insufficiency that presents as nausea associated with hypotension and abdominal cramps.[5]

Intracranial and Other Causes of Nausea

Some patients who are at the end of life experience nausea related to intracranial factors, including swelling, bleeding, tumors, and meningitis.[3,5] These patients tend to experience nausea and vomiting, especially in the morning, with headaches.[3] The clustering of fear and/or anxiety with nausea and small volumes of vomiting can occur.[5]

When movement induces or exacerbates nausea, especially when accompanied by vertigo and imbalance, the cause may be vestibular in nature, such as in Meniere disease or chronic vestibular dysfunction.[3,11] Hormonal and metabolic alterations related to advanced cancer, renal and/or liver failure, and fluid and nutritional deficits can also lead to nausea.[2] For example, hypercalcemia, a common complication of advanced cancer that occurs in 10% to 20% of patients, can cause nausea and vomiting; an associated dehydration and constipation can also induce or exacerbate nausea.[12] Hyponatremia in patients with congestive heart failure or kidney failure, uremia due to kidney failure, or infection such as esophagitis, gastroenteritis, and sepsis can also lead to nausea.[2,5] Likewise, excessive oropharyngeal secretions and coughing can cause nausea, with or without vomiting.[2,5,13,14] Finally, gastroparesis experienced by patients with diabetes and constipation and nutritional deficits related to poor oral intake secondary to debility or dementia contribute to this symptom.[3]

PATHOPHYSIOLOGY

The neurophysiology of nausea and vomiting is complex, involving numerous receptors and circuitry in several areas throughout the body, not all of which have been well elucidated.[1,3,15] Nausea is believed to include more cerebral involvement and consciousness than vomiting, in which a reflex action is triggered by the lower brain structures.[2] A specific anatomical area related to nausea and vomiting is the "vomiting center" (VC) in the medulla, which has receptors for histamine, acetylcholine, dopamine, and serotonin.[1]

The VC integrates signals from the other neuronal areas to coordinate the emetic response. These include the cerebral cortex, the limbic system and thalamus, the vestibular nuclei/cerebellum, the chemoreceptor trigger zone (CTZ) in the fourth ventricle of the brain, and, in the periphery, the GI tract.[1,2,15] The cerebral cortex has multiple chemoreceptors, including γ-aminobutyric acid, dopamine, serotonin, acetylcholine, and neurokinin-1 (NK-1) receptors that are activated by factors such as smells, anxiety, and pain. Mechanoreceptors are also involved, sensitive to mechanical pressure from the stretching and irritation of the meninges that can occur with infection, swelling, or an intracranial mass. Histamine and cholinergic receptors in the cerebellum may be activated by opioids and afferent input from the inner ear. The CTZ, which is unprotected by the blood-brain barrier and therefore exposed to agents within the bloodstream such as opioids, metabolites, and toxins, has the serotonin 3, dopamine, histamine, and NK-1 receptors, which are sensitive to these agents.[1,13,15,16] These same receptors are activated by neurotransmitters released from enterochromaffin cells in the GI tract when they are exposed to medications, toxins, and radiation.[2,17] Histamine and cholinergic mechanoreceptors in the GI system are activated by distortion induced by gastroparesis, bowel obstruction, and metastases/masses in the GI tract and peritoneum.[2,17] Activation of GI receptors leads to signaling via vagal afferents that either directly innervate the VC or innervate the VC via the CTZ.[2,17] Similarly, oropharyngeal irritation can stimulate the CTZ via histamine and acetylcholine-activating vagal afferents.[2,17]

Treatment of nausea can be based on an understanding of these receptors. Dopamine is most commonly targeted when managing nausea outside the chemotherapy setting,[14] because the dopamine receptor (1) is better studied, (2) is present in several of the centrally located nausea signaling centers such as the VC where signals are integrated and the CTZ that is exposed to systemic toxins and medications, and (3) is present peripherally in the GI tract where it mediates nausea caused by gastroparesis, constipation, and bowel obstruction. The mnemonic "VOMIT" (Vestibular apparatus, Obstruction, Motility/Mind, Infection/Inflammation, and Toxins/Tumor) can remind providers about possible etiologies of nausea.[18] Although this mnemonic does not include receptors involved in nausea, it may prompt the provider to investigate some of the common causes of nausea experienced by patients at the end of life.

PATIENT ASSESSMENT

A thorough history and patient examination are essential in attempting to uncover a likely cause(s) of nausea that then guides management. Characteristics of nausea including its frequency, duration, severity, and related vomiting are noted. Patient-reported tools, such as the numeric 0 to 10 rating scale or the Edmonton Symptom Assessment Scale that provides the means of assessing nausea alongside other commonly distressing symptoms, can be used.[1,4] Functional status, symptom burden, and goals of care are also assessed by speaking with the patient and/or proxy. Physical examination findings are noted. Weight change and the presence of postural hypotension may suggest fluid and electrolyte imbalances related to nausea. Abdominal distension with or without hypoactive or absent bowel sounds, tenderness, and/or masses and fecal impaction are other common causes of nausea.[2]

Laboratory testing may include a complete metabolic panel, liver enzymes, and urea or bilirubin. Radiologic examinations may be indicated if obstructions or other pathology is expected; findings may lead to therapeutic approaches that can alleviate the burden of this symptom at the end of life.[2,3]

TREATMENT STRATEGIES

Many antinausea medications were developed to manage chemotherapy-induced nausea and vomiting. However, most of these have not been scientifically evaluated in the end-of-life population; providers have needed to instead rely on expert consensus and experience. Classes of medications to combat nausea include dopamine antagonists, serotonin antagonists, histamine antagonists, muscarinic acetylcholine receptor antagonists, NK-1 receptor antagonists, and cannabinoids. For example, the dopamine receptor can be targeted with the use of a prokinetic agent such as metoclopramide in a patient with constipation; the histamine receptor can be targeted in a patient who has motion-associated nausea. Specific agents and indication for use are listed in the Table; those that are used only to relieve chemotherapy-related nausea, such as the NK-1 receptor antagonists, have been excluded. Antinausea medications may have broad activity because the receptors that mediate nausea, especially dopamine and serotonin receptors, are located in numerous places. If the cause of nausea cannot be determined initially, different agents can be tried for short periods or agents from different classes can be combined.[2,3,14,18] Of note, combination antinausea therapy may not be any more efficacious than monotherapy in patients with advanced cancer.[5]

Dopaminergic Antagonists

Outside the chemotherapy setting, nausea is thought to largely be due to signaling via the dopamine receptor.[14] The following antidopaminergics target this receptor and may be used; however, providers must also consider common adverse effects including extrapyramidal symptoms (EPS) such as tardive dyskinesia, Parkinsonism, and dystonia.[9,16] Haloperidol is commonly used to manage nausea, although a review of randomized controlled trials (RCTs) in the palliative care setting does not provide strong evidence for its efficacy.[5,19] Prochlorperazine may be used in patients with nausea caused by gastroparesis or involvement of the CTZ,[3,14] although efficacy in the end-of-life setting is unknown.[5] Likewise, levomepromazine may be useful in patients whose nausea is multifactorial and in those who are refractory to other agents, because this medication targets several receptors,[15] but RCT evidence for its efficacy is lacking.[20] Olanzapine, a second-generation atypical antipsychotic that targets the serotonin receptor 3 and histamine receptor sites, may be selected when the cause of nausea is unknown, when other agents have been attempted, and/or when EPS are present.[16,21-25]

Metoclopramide

Metoclopramide is an agent deserving of its own category in the treatment of nausea. Unlike other more centrally acting dopamine antagonists, metoclopramide works primarily at the dopamine receptors in the GI tract, with some effects on the CTZ.[3,16] In the GI tract, metoclopramide also antagonizes serotonin 3 receptors, activates serotonin 4 receptors, and enhances release of acetylcholine, leading to the activation of the muscarinic receptors and thus peristalsis in the stomach and small bowel.[3,14] For these reasons, metoclopramide can be particularly beneficial in patients who have nausea related to GI causes. Metoclopramide is the only prokinetic agent approved for use in the United States and is often a first-line therapy in patients with gastroparesis.[3] Consensus guidelines by the Multinational Association of Supportive Care in Cancer recommend metoclopramide as the drug of choice for use in advanced cancer patients without bowel obstruction; however, the medication is contraindicated in patients with GI bleeding and perforations.[5] Because of the risks for EPS, metoclopramide is not approved by the US Food and Drug Administration for use for more than 12 weeks and must be used with extreme caution in frail older adults.[2,3]

Serotonin Antagonists in the Setting of Palliative Radiation Therapy

Serotonin antagonists, the "setrons," namely, ondansetron and granisetron, work by antagonizing the serotonin 3 receptor in numerous places.[3] These agents are recommended for the nausea prophylaxis locally in the GI tract due to cancer therapy[26] and to control the accumulation of serotonin that occurs with bowel obstructions.[2] The secondary effects of the "setrons" centrally also allow for the control

TABLE Antinausea Agents for Consideration in End-of-Life Care

Antinausea Agent	Indications	Suggested Regimen	Adverse Effects/ Contraindications
Dopamine receptor antagonists			
Butyrophenone Haloperidol (Haldol)	Opioid-induced nausea, chemical/metabolic nausea, bowel obstruction	PO: 1.5-5 mg q4-6 h SC: 1-5 mg/d via continuous SC infusion IV: 0.5-2 mg q3-4 h	More EPS
Prokinetic agents Metoclopramide (Reglan, Metozolv ODT)	Gastric stasis, partial bowel obstruction, drug of choice in advanced cancer	PO, ODT, IV: 10-30 mg q4-6 h	Restlessness, sedation, fatigue, EPS, esophageal spasms, GI colic Use cautiously in older adults, higher doses, not approved for use more than 12 wk or with complete bowel obstruction
Phenothiazines Prochlorperazine (Compazine)	Treatment of nausea and vomiting of various causes	PO: 5-25 mg q4-6 h Rectal: 25 mg q6-8 h IM: 5 mg/mL q3-4 h IV: 20-40 mg q4-6 h	EPS, anticholinergic symptoms, sedation, anxiety, IM route may cause pain
Levomepromazine	Refractory nausea in palliative care	PO: 6.25-25 mg q12 h SC: 25-50 mg/d	More sedative, anticholinergic effect, administer cautiously in renal, hepatic impairment, second- or third-line therapy in palliative care, has analgesic properties
Olanzapine (Zyprexa, Zydis)	Refractory nausea, nausea in cancer patients	PO: 2.5-10 mg q12-24 h	Sedation, reduced seizure threshold, increased serum lipids and glucose QT prolongation
Serotonin receptor 3 antagonists			
Ondansetron (Zofran)	Chemotherapy and radiation-induced nausea	PO/ODT: 4-8 mg q8-12 h IV: 0.15 mg/kg q12 h	Constipation, headache, clinical efficacy plateaus
Granisetron (Kytril, Sancuso)		PO: 1 mg q12 h 7-d transdermal patch: 3.1 mg/24 h IV: 10 mcg/kg q12 h	
Histamine receptor antagonists/antihistamines			
Diphenhydramine (Benadryl)	Vestibular and central nervous system causes	PO/IV: 12.5-50 mg q6-8 h	Anticholinergic effects, dry mouth, blurred vision, sedation (less with cyclizine), constipation
Hydroxyzine (Atarax)		PO/rectal/IV: 12.5-25 mg q6-8 h (max dose, 100 mg/d)	
Cyclizine (meclizine)		PO/SC: 25-50 mg q8 h (max dose, 200 mg/d)	
Muscarinic acetylcholine receptor antagonists/anticholinergic			
Hyoscine (scopolamine)	Advanced cancer, vestibular mechanisms	SL: 200-400 mcg q4-8 h SC: 200-400 mcg q4-6 h Cont. SC infusion: 80-120 mcg/d Transdermal: 500-1500 mcg q72 h	Dry mouth, constipation, ileus, urinary retention, blurred vision, agitation, onset of action of 24 h

(continues)

TABLE Antinausea Agents for Consideration in End-of-Life Care, Continued

Antinausea Agent	Indications	Suggested Regimen	Adverse Effects/ Contraindications
Other agents			
Anxiolytics Lorazepam	Anxiety	PO/IV: 0.5-1 mg q6-24 h	Not FDA approved as antiemetic
Corticosteroids Dexamethasone	Chemotherapy- and radiation-induced nausea, advanced cancer, increased intracranial pressure, malignant bowel obstruction	PO/IV: 2-4 mg q6-24 h	Infection risk, insomnia, anxiety, euphoria, perirectal burning (IV route), hyperglycemia
Sandostatin analogues Octreotide (Sandostatin 50 mg/mL)	Malignant bowel obstruction, intractable vomiting	SC: 100-150 mg q8 h Cont. IV infusion: 0.2-0.9 mg/d IM depot: 20-30 mg q3-4 wk	Pain at injection site Reduces peristalsis, secretions, dose reduced with renal, hepatic impairment

Abbreviations: Cont, continuous; EPS, extrapyramidal symptoms; FDA, US Food and Drug Administration; IM, intramuscular; IV, intravenous; ODT, oral dissolving tablet; PO, oral; SC, subcutaneous; SL, sublingual.[2,3,5,16]

of opioid-related nausea and prolonged nausea that can occur with serotonergic syndromes such as renal failure.[3,26]

Palliative radiation therapy (RT), particularly when delivered in a single fraction, may be appropriate at the end of life to alleviate symptoms from conditions such as brain and bone metastases.[27,28] However, nausea and vomiting are common adverse effects of RT, and rates of nausea in this population continue to be high despite antiemetic prophylaxis.[29] The use of other antiemetics such as the NK-1 antagonists and corticosteroids, along with serotonin antagonists, has been found to improve the management of nausea in patients receiving moderately emetogenic RT for bone metastases.[30,31]

In patients at the end of life with nausea not caused by RT, serotonin antagonists are used predominantly as second- or third-line agents because their clinical efficacy plateaus over time and they tend to be more expensive.[3,14,16] When nausea is associated with vomiting, the oral disintegrating tablet version of ondansetron or the transdermal patch version of granisetron may be considered. Regardless of the delivery method, the use of serotonin antagonists needs to be evaluated because they can exacerbate the prevalent symptom of constipation.[15,16]

Antihistamines

Histamine antagonists include diphenhydramine, hydroxyzine, and cyclizine. These agents block the histamine receptors in the vestibular nucleus, cerebral cortex, CTZ, and VC and therefore are not only effective for movement-induced nausea but also for nausea caused by increased intracranial pressure and CTZ irritation, such as with opioids.[3,5] All 3 drugs are sedating and have anticholinergic adverse effects including blurred vision, headaches, confusion, constipation, and urinary retention; diphenhydramine and hydroxyzine especially should be used with caution in the elderly population.[2,3,14,18]

Cyclizine, having greater antimuscarinic activity, is more effective at reducing mucosal secretions, making it theoretically appropriate in the setting of bowel obstruction.[5,18] Although current guidelines support the use of cyclizine in the palliative care population, there is limited evidence to back these recommendations.[5,15] Of note, cyclizine cannot be used with metoclopramide because of competition for the same set of receptors.[3,15]

Anticholinergics

Scopolamine is an anticholinergic agent that can be used for a range of indications including nausea resulting from increased intracranial pressure, intestinal obstruction, and oropharyngeal secretions. This drug works both centrally in the VC and peripherally on the muscarinic receptors.[2,3,14] Transdermal scopolamine allows delivery of medication over a period of 3 days, but it may not be appropriate for acute management because it can take about a day to realize therapeutic effects.[2,26] Both the oral and transdermal forms of scopolamine can be used alone or in combination with other antinausea agents.[14]

Other Agents

The anxiolytic lorazepam, the corticosteroid dexamethasone, and the somatostatin analog octreotide can be used independently or in combination with others listed previously. Lorazepam is not approved by the US Food and Drug Administration as an antinausea or antiemetic agent, but because it acts on the cortical structures to manage nausea related to anxiety, it can be effective for anticipatory nausea.[2,3,14] Dexamethasone works via the central corticosteroid receptors in a yet-unclear mechanism with variable

efficacy.[3] In practice, dexamethasone is seldom used as a first-line therapy because of the increased risk for infection and sepsis and the need for tapering to minimize withdrawal symptoms and adrenal insufficiency.[2,3,16] Although temporarily effective in relieving increased intracranial pressure, headaches, and nausea in patients with glioma, dexamethasone is also thought to be inappropriate at the end of life because the withdrawal of steroids is not associated with an increase in symptom severity.[32] Palliative care experts generally consider steroid use as potentially inappropriate in the last days of life; in contrast, haloperidol, metoclopramide, and levomepromazine are deemed more appropriate.[33]

Octreotide is not considered an antinausea agent, but it may help reduce nausea, vomiting, and pain in patients with complete bowel obstructions. Octreotide acts on somatostatin receptors in the brain, pituitary gland, and GI tract to reduce vasopressin and gastrin secretion, in turn reducing GI secretions and peristalsis and decreasing obstructive symptoms.[2,34] Octreotide may be more effective than scopolamine.[2] However, likely because of only low-level evidence for its benefit in malignant bowel obstruction,[34] current consensus guidelines recommend that octreotide be used with another antiemetic to manage nausea and vomiting in advanced cancer patients with malignant bowel obstruction.[5]

In summary, selecting an antinausea agent at the end of life is dependent on the likely cause of nausea; an understanding of the related pathophysiology is essential. Generally, a single medication is optimized for therapeutic effect at reducing nausea, before another agent from a different class is added.[13,14] The provider must address underlying reversible causes of nausea including constipation, dehydration, hypercalcemia, and adverse effects from medications. For example, a bowel program must be initiated when an opioid is prescribed.

Nonpharmacologic Treatments

Although pharmacological interventions are often the first-line approach to manage nausea, some nonpharmacological interventions may help alleviate this symptom. For example, if certain sounds, smells, sights, foods, and motion exacerbate nausea, these should be avoided.[2] Guidelines from the National Comprehensive Cancer Network suggest palliative RT to the brain to relieve nausea caused by brain metastases and referral to mental health providers for patients with suspected psychogenic causes of nausea.[35]

Interventions including surgery for nausea caused by bowel obstruction tend not to yield significant gains for patients near the end of life regardless of the type of surgical technique used or position of obstruction.[14] Particularly in patients with multiple obstructions, poorer performance status related to age, metastases, ascites, and cachexia, such invasive methods may in fact result in painful complications incongruent with the goals of care at the end of life.[14] In patients at a high risk for surgical complications, the endoscopic or radiological insertion of percutaneous venting gastrostomy tubes and enteral stents may offer relief of nausea and other symptoms associated with bowel obstructions; however, these are not without their own risks including migration, perforation, and obstruction.[14] Such interventions may be inconsistent with patient preferences and goals of care.

Because oral or intravenous fluids of more than 1 L/d may improve nausea, hydration can be a part of the treatment regimen as long as the patient does not have pain, abdominal distension, and vomiting—all symptoms indicative of bowel obstruction.[14] Hypodermoclysis, a simple but underused method of administering hydration via the subcutaneous route, has also been recommended in the treatment of nausea near the end of life because it has several advantages over the intravenous route including less cost and lower risk for infection and blood clots.[14,36]

Complementary and alternative therapies may be considered for the management of nausea, including relaxation, imagery, distraction, and self-hypnosis; integrative therapies such as acupuncture, acupressure, ginger, and aromatherapy might also be suggested.[2] Many of these therapies have primarily been studied in patients who experience nausea and vomiting after chemotherapy[37,38]; there is little evidence that they relieve nausea from other etiologies. Although the evidence for complementary approaches in the management of nausea per se in patients at the end of life is not strong, providers may consider them especially if requested by patients.

ROLE OF PROVIDERS IN TIMELY ASSESSMENT AND DISCUSSIONS ABOUT PREFERENCES

The multifactorial nature of nausea and its prevalence at the end of life, as well the lack of well-designed studies in the end-of-life population about management of this symptom, are clear. Added to these challenges are inadequate assessment of nausea, the use of antinausea medications that are inappropriate, and late referral to hospice. However, admission to hospice in itself should not be viewed as a magic bullet. A recent longitudinal cohort study of more than 149 000 Medicare beneficiaries served by 577 hospices led to the finding of variations in quality of care between hospices that affected where patients died and whether they received intensive therapy at the end of life.[39] When patients expressed their preference regarding site of death, a significant reduction of emergency department visits and hospitalization was noted; likewise, more frequently monitored symptoms led to a reduction in intensive medical care.

Information sharing can be particularly helpful in reducing distress and increasing the control patients and families experience. Early on in the palliative care or hospice trajectory, the provider should provide information on recognizing the signs of nausea and associated symptoms, how and when to give/take medications, adverse effects to watch out for, and what to do if current management is inadequate.[2] Having a plan and someone with experience and knowledge to turn to for guidance may reduce the sense of helplessness that patients and families may experience and empower them at a time when such support is most required.

The relative scarcity of evidence regarding the management of nausea in the end-of-life population has led to management practices that may not be adequate in controlling this common and troublesome symptom. Although it is understandably challenging to perform RCTs in this vulnerable patient population, larger, well-designed controlled studies that compare different agents may offer stronger evidence about treatment options, leading to improved outcomes.

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