Practical Management of Chemotherapy-Induced Nausea and Vomiting

By Wendy Wiser, DO and Ann Berger, MSN, MD

Approximately 70% to 80% of all patients who receive chemotherapy experience nausea and vomiting, which can disrupt their lives in numerous ways. Chemotherapy-induced nausea and vomiting (CINV) has traditionally been classified according to three patterns: acute, delayed, and anticipatory. Additional classifications include refractory and breakthrough nausea and vomiting. The mechanisms by which chemotherapy causes nausea and vomiting are complex, but the most common is thought to be activation of the chemoreceptor trigger zone. An appreciation of the risk factors for developing CINV is important when matching antiemetic treatment to risk. The emetogenicity of the chemotherapy regimen—generally categorized as high, moderate, low, or minimal—greatly affects a patient’s risk for developing CINV. In addition to established and emerging pharmacologic approaches to managing CINV, many complementary and integrated modalities may be options. Progress in CINV management must include a better understanding of its etiology and a focus on prevention. This review will consider the etiology, assessment, and treatment of patients with CINV.

A practical issue in every oncology practice is the management of chemotherapy-induced nausea and vomiting (CINV). For the patient it is a quality-of-life issue, and for the medical team caring for the patient, the importance of addressing CINV can not be overstressed. As new drugs such as palonosetron (Aloxi) and aprepitant (Emend) emerge, we as clinicians can best serve our patients with an improved understanding of the pathophysiology of CINV. In light of the multifactorial nature of CINV, it is also important to be comfortable with evaluation and diagnosis of this debilitating syndrome. In addition to the pharmacologic approaches, many complementary and integrated modalities may be options for the person with CINV. Future progress in CINV management must include a better understanding of its etiology and a focus on prevention in order to offer maximal symptom control.

Definitions and Prevalence

Nausea is a symptom. It is a subjective, unpleasant experience associated with flushing, tachycardia, and the urge to vomit. Vomiting is a physical phenomenon that involves contraction of the abdominal muscles, descent of the diaphragm, and expulsion of stomach contents. As a selfprotective mechanism, vomiting can sometimes expel noxious substances from the body. Approximately 70% to 80% of all patients who receive chemotherapy experience nausea and vomiting.[1] Anticipatory nausea and vomiting are experienced by approximately 10% to 40% of patients who receive chemotherapy.[1] Nausea and vomiting remain two of patients' most feared effects of cancer treatment, and few side effects of chemotherapy are as universally reported. One early study from 1983 found that vomiting and nausea were the first and second most severe effects of chemotherapy, respectively. Nausea and vomiting consistently rank among the top three reported side effects, along with alopecia. Additionally, many other reported medical side effects, such as weight loss (ranked as number 11), loss of appetite (number 16), and increased thirst (number 37), can result from nausea and vomiting.[1]

Quality-of-Life Issues

TABLE 1
Chemotherapy-related nausea and vomiting can be disruptive to a person's life in various ways. It can negatively affect a patient's ability to perform activities of daily living. Lindley et al noted degeneration of self-care and decrease in functional, psychological, and physical quality of life in patients receiving intermittent bolus chemotherapy regimens on an outpatient basis (Table 1).[6] CINV can negatively affect a person's overall health and lead to withdrawal from potentially useful or curative treatment. Loss of appetite is a common effect of nausea and vomiting, as well as a direct effect of some chemotherapeutic agents. Loss of appetite can lead to malnutrition and weight loss or even anorexia. Dehydration is a related concern. The medical team and caregivers must work closely with a dietitian to monitor and help plan strategies to counter these issues.[7] In addition to metabolic derangements and depressed mood, CINV is also associated with fatigue and insomnia. The reasons for this are unclear, but one component of this phenomenon is likely the psychological stress of constant nausea and vomiting. Dyspnea and constipation have also been associated with CINV, although the reasons for these symptoms are not clear.[7]

**Assessment**

When assessing the symptoms of nausea and vomiting, the two should be assessed separately. It is recommended that the clinician ask questions about the nausea concerning, for example, the severity and duration, time of day, and other mitigating factors. When assessing emesis, the number of episodes and duration of vomiting, as well as the contents and color of the vomitus (i.e., pills, whole undigested food, coffee ground, bilious, etc) can be very helpful information. The inability to keep down other oral therapy such as pain medication can only compound how terrible the patient is feeling from the nausea and vomiting, and alternate medication routes may need to be discussed until nausea and emesis are better controlled. Chemotherapy-induced nausea and vomiting has traditionally been classified into three categories based on the time of onset and pattern of occurrence in relation to the time of chemotherapy administration [8]. These three patterns are acute, delayed, and anticipatory nausea and vomiting. Two additional types associated with lack of symptom control are refractory and breakthrough nausea and vomiting. Chemotherapy-induced nausea and vomiting has traditionally been classified into three categories based on the time of onset and pattern of occurrence in relation to the time of chemotherapy administration [8]. These three patterns are acute, delayed, and anticipatory nausea and vomiting. Two additional types
associated with lack of symptom control are refractory and breakthrough nausea and vomiting. Acute CINV refers to nausea or vomiting, or both, that occurs during the first 12 to 24 hours after the administration of chemotherapy; symptoms generally peak after 5 to 6 hours.[9] Cisplatin in high doses (50-120 mg/m²) will cause emesis in 90% of patients who are not taking prophylactic antiemetics within 24 hours of administration.[10] Most emetogenic chemotherapeutic agents induce emesis about 1 to 2 hours after administration. Acute CINV is the most researched type. The treatment is mainly pharmacologic, and control is still problematic despite improved medication options.[11] Delayed CINV occurs 24 hours after chemotherapy administration. Delayed CINV may last for 6 or 7 days. Acute and delayed CINV are inextricably linked, as the prevention of acute symptoms invariably prevents delayed symptoms. Postulated mechanisms for delayed CINV are different from those for acute CINV. Delayed CINV is well defined when it occurs after high doses of such compounds as carboplatin, doxorubicin, epirubicin (Ellence), and anthracyclines. Cisplatin is associated with approximately a 65% to 90% likelihood of causing delayed emesis in the absence of antiemetic prophylaxis.[12] Anticipatory CINV refers to nausea or vomiting as a learned or conditioned response that typically occurs before the administration of chemotherapy. In this situation, patients may be responding to a variety of stimuli such as odor, sight, or sound that is usually associated with a prior experience in which emesis was inadequately controlled. The corresponding psychological mechanism for anticipatory emesis is unknown and is secondary to the direct administration of the chemotherapeutic agent itself. Thus, patients must be given the opportunity to receive the optimal antiemetic regimen with their initial course of chemotherapy to prevent acute CINV as well as anticipatory CINV. Breakthrough nausea and vomiting refers to symptoms that occur despite antiemetic preventive therapy and that necessitate the use of rescue medications. No clear consensus on treatment protocol for this phenomenon exists, although guidelines have been set forth by the National Comprehensive Cancer Network (NCCN).[8,13]

**Pathophysiology**

Mechanisms by which chemotherapeutic agents cause nausea and vomiting are complex. The most common is thought to be activation of the chemoreceptor trigger zone (CTZ) located in the area postrema in the floor of the fourth ventricle. Other mechanisms are peripheral stimulation of the gastrointestinal (GI) tract via the vagus nerve, higher centers of the brain stem, and cortex; alterations of taste or smell; and vestibular events via cranial nerve VIII.[1,14] Afferent input from these triggers are perceived by an area in the medulla oblongata known as the vomiting center. Specific neurotransmitters linked to neuroreceptors in the GI tract and CTZ, when activated or irritated by a chemotherapeutic agent, can send input to the vomiting center.[15] Antiemetic therapy targets neuroreceptors located in the peripheral and central nervous system that can activate this central processing area of the brain. The exact neurophysiology of CINV remains unclear. The CTZ is activated via blood or cerebrospinal fluid and invokes the release of various neurotransmitters, which stimulate the vomiting center. Peripherally, when a chemotherapeutic agent causes irritation and damage to GI mucosa, the result is a release of neurotransmitters. These neurotransmitters activate receptors, which in turn send signals to the vomiting center via the vagal afferents. Structurally, parasympathetic stimulation (via cranial nerve X) will increase the secretion rate of almost all GI glands.[1,12,16] Once activated, the vomiting center modulates the efferent transmission to the respiratory, vasomotor, and salivary centers as well as to the abdominal muscles, diaphragm, and esophagus, resulting in emesis. Clearly, the neurophysiology of vomiting is complex and only just beginning to be understood.

**Neurotransmitters and Receptors**

**TABLE 2**

<table>
<thead>
<tr>
<th>Input Triggers for Emesis at the Level of the Medulla Oblongata</th>
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Numerous neurotransmitters are known to have a role in CINV. These include serotonin, substance P, histamine, dopamine, acetylcholine, gamma-aminobutyric acid (GABA), and enkephalins (Table 2). Any one or a combination of these transmitters may induce vomiting. Other enzymes surround the CTZ, such as adenosine triphosphatase, monoamine oxidase, cholinesterase, and catecholamines; however, their role in chemotherapy-induced emesis is unknown. The serotonin/5-HT3-receptor pathway as well as the substance P/NK1 receptor pathway play major roles in the modulation of CINV. The significance of the serotonin (5-HT3 receptor) pathway was first recognized with high-dose metoclopramide in decreasing cisplatin-induced emesis. Metoclopramide is a weak antagonist of peripheral 5-HT3 receptors and can stimulate GI motility by increasing acetylcholine release from the cholinergic nerves of the GI tract. The introduction of 5-HT3-receptor antagonists offered an improved treatment option for CINV. Their precise mechanism of action is unknown, but their primary mechanism of action appears to be peripheral. Serotonin receptor antagonists are most effective for acute vomiting but have variable efficacy in delayed CINV, with the exception of a new 5-HT3-receptor blocker, palonosetron. Substance P (mediated by NK-1 receptors) is known to modulate nociception to the brain. High-density NK-1 receptors are located in the regions of the brain implicated in the emetic reflex. The primary mechanism of NK-1-receptor blockade appears to be central, and NK-1 antagonists are effective for both acute and delayed events. These agents augment the antiemetic activity of 5-HT3-receptor antagonists plus corticosteroids in the prevention and treatment of CINV. Histamine receptors are found in abundance in the CTZ; however, H2 antagonists do not work well as antiemetics. H1 antagonists help to alleviate nausea and vomiting induced by vestibular disorders and motion sickness. In the recent past, the neurotransmitter that appeared to be most responsible for chemotherapy-induced nausea and vomiting was dopamine. Many effective antiemetics are dopamine antagonists that may bind specifically to the D2 receptor. However, there is a high degree of variation in the dopamine receptor-binding affinity of these drugs. The action of some drugs that cause nausea and vomiting is affected very little or not at all by the dopamine antagonists. Not all the important receptors in the CTZ are dopaminergic, as the effect of dopamine antagonists is not equal to surgical ablation of the CTZ. It has also been noted that the degree of antiemetic activity of high-dose metoclopramide cannot be explained on the basis of dopamine blockade alone. Metoclopramide is a weak antagonist of peripheral 5-HT3 receptors and can stimulate GI motility by increasing acetylcholine release from the cholinergic nerves of the GI tract. Opiate receptors are also found in the CTZ. It is known that narcotics have mixed emetic and antiemetic effects that are blocked by naloxone. Naloxone also has emetic properties. These facts have led to the proposal of using opiates and enkephalins as antiemetics.

Other Mechanisms

Other mechanisms that may be involved in CINV are effects directly or indirectly on the cerebral cortex, olfactory or gustatory stimuli, and effects on the vestibular system. Animal studies have shown that nitrogen mustard partially causes emesis via direct stimulation of the cerebral cortex. Other evidence indicates that indirect psychological effects can mediate CINV; for example, the risk of nausea and vomiting may increase if the patient's roommate is experiencing nausea or vomiting, and the amount of sleep before receiving chemotherapy may influence whether a patient develops chemotherapy-induced emesis. The importance of taste and odor perception in relation to enhancement of gagging, nausea, and vomiting is well appreciated, although the exact mechanism is unknown. Women who have suffered from hyperemesis during pregnancy show taste damage. In a study of breast cancer patients who received cyclophosphamide, methotrexate, and fluorouracil, 36% reported a bitter taste in their mouth. A third of the patients believed this bitter taste led to vomiting. Clearly, changes in taste may contribute to both nausea and vomiting as well as to anorexia. Chemotherapeutic agents can also cause CINV by influencing the vestibular system. Patients with a history of motion sickness or vertigo experience a greater severity, frequency, and duration of nausea and vomiting from chemotherapy than patients who do not experience motion sickness or vertigo. Once again, the mechanism by which effects on the vestibular system may lead to CINV is unknown, but it is postulated that sensory information received by the vestibular system differs from information that was anticipated.

Patient Risk Factors

An appreciation of the risk factors for developing CINV is important when matching antiemetic
treatment to risk. Prognostic indicators for developing chemotherapy-induced nausea and vomiting include those that are intrinsic to the patient, the chemotherapy, or the tumor. Patient characteristics that may affect antiemetic control include prior experience with chemotherapy, alcohol intake history, age, and gender. A previous experience with chemotherapy often sets the stage for success or failure in controlling emesis during future courses of chemotherapy. Giving the appropriate antiemetic medication as part of the plan during the initial course of chemotherapy often eliminates the subsequent chance of anticipatory CINV (and may decrease the severity of delayed emesis). Other patient-specific risk factors exist. Chronic and heavy alcohol intake (ie, > 100 g of ethanol or five mixed drinks per day), whether past or current, has been shown to positively affect the control of emesis.[1] In contrast, someone who is sensitive to the effects of drinking alcohol (eg, feeling warm, drowsy, or nauseous) with relatively light or rare intake might have a higher chance of experiencing CINV. As a prognostic indicator, age cannot predict patient response to chemotherapy, but the tendency is that the younger the patient, the sicker he or she will become. Gender is another patient factor in considering risk for CINV. For unknown reasons, women achieve poorer control of emesis during treatment for various malignancies. A possible explanation might be that women tend to more often receive chemotherapy regimens with highly emetogenic agents such as cisplatin and cyclophosphamide, usually given together. Women are also less likely than men to have a history of high alcohol intake.[1] Other contributing factors that may affect the control of emesis include fatigue, low social functioning, personal history of motion sickness, hyperemesis with pregnancy, anxiety, and prechemotherapy nausea [1,7].

Emetogenicity of Drugs

TABLE 3

<table>
<thead>
<tr>
<th>Risk for Emesis With Commonly Used Chemotherapy Drugs*</th>
<th>Risk Level</th>
<th>Percentage</th>
</tr>
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<tbody>
<tr>
<td>Risk Level of Emesis</td>
<td>Drug (mg/m²)</td>
<td>Emesis</td>
</tr>
<tr>
<td>Low</td>
<td>cisplatin (50-100 mg/m²)</td>
<td>10-30%</td>
</tr>
<tr>
<td>Moderate</td>
<td>cisplatin (100-300 mg/m²)</td>
<td>30-50%</td>
</tr>
<tr>
<td>High</td>
<td>cisplatin (≥300 mg/m²)</td>
<td>&gt; 50%</td>
</tr>
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Certainly the emetogenicity of the regimen used greatly affects a patient’s risk for developing chemotherapy-related nausea and vomiting. At least four different categories of emetogenic potential exist—high, moderate, low, and minimal—depending on the classification system one references (as there is no universal consensus on one classification system for the emetogenicity of cancer chemotherapy). That said, the emetogenicity of different agents is clearly diverse, which is one of the most important tools we have in the prevention and treatment of CINV (Table 3).[21] Of note is cisplatin, the prototype chemotherapy for emetogenic risk level 5 (meaning the drug is associated with more than a 90% chance of emesis in the absence of effective antiemetic prophylaxis). More importantly, cisplatin is the cornerstone of therapy for many cancers, yet poses a universal risk (> 99%) of emesis at doses less than or equal to 50 mg/m². It has a well characterized emetogenic profile that serves as a model for antiemetic testing. Thus, if an antiemetic is efficacious against the CINV of cisplatin, this can be predictive of antiemetic efficacy with other chemotherapeutic drugs.
Treatment

The goals of therapy in the management of CINV are to enhance the patient's quality of life, eliminate nausea and vomiting, provide convenient care, reduce hospital and clinic time, and reduce treatment costs. The principal strategy for management of CINV is prevention. This concept of prevention is similar to that in pain management and more effective than salvage therapy. A goal of prevention reduces morbidity and medical complications and is cost-effective. Consequently, patients are more likely to complete treatment. It is important to be aware of the current antiemetic agents and thoughts for guiding their use to prevent and treat CINV. There is a growing diversity of antiemetic classes. As more is known about the causes and modulators of CINV, one can anticipate the antiemetic guidelines to evolve as well. As discussed previously, the five known neurotransmitter receptor sites of primary importance in the vomiting reflex are M1 (muscarinic), D2 (dopamine), H1 (histamine), 5-hydroxytryptamine (5-HT)-3 (serotonin), and neurokinin 1 (NK) receptor (substance P). Consequently, the current antiemetic drug classes are anticholinergics (primarily for motion sickness prophylaxis), dopamine-receptor antagonists (phenothiazines, butyrophenones, and benzamides), antihistamines (primarily for motion sickness), serotonin-receptor antagonists, and the relatively new neurokinin-1-receptor antagonists. Three other general antiemetic classes with less well understood mechanisms of action are the corticosteroids, cannabinoids, and benzodiazepines.

Most Active Antiemetics

The antiemetic agents considered to be most active for the management of CINV are the type 3 serotonin (5-HT3)-receptor antagonists, corticosteroids, and metoclopramide, which has substantial antagonism at both serotonin- and dopamine-receptor sites. Of note is palonosetron, a second-generation 5-HT3 antagonist that is currently the only Food and Drug Administration (FDA)-approved serotonin antagonist for the prevention of delayed CINV with moderately metemocogenic chemotherapy.[22]

• Serotonin Antagonists—The antiemetic activity of metoclopramide is thought to be a serotonin antagonist, although substantial dopaminergic antagonist action exists as well. This explains the potential for extrapyramidal reactions. One must recognize the potential that exists for acute dystonic reactions in the setting of dopamine-receptor blocking agents such as phenothiazines (prochlorperazine, chlorpromazine, thiethylperazine [Torecan]), butyrophenones (droperidol, haloperidol), and substituted benzamides (metoclopramide). This alarming side effect is usually characterized by trismus or torticollis. Within the patient population under age 30, chemotherapy that might call for antiemetic prophylaxis is often given over several consecutive days, thus increasing the possibility of acute dystonic reactions.[1] The fact that 5-HT3 antiemetic agents do not cause acute dystonic reactions makes them an especially helpful treatment option for children and younger adults. In light of the possible side effects of metoclopramide, other treatment options were developed with a specific focus on blocking the serotonin receptor. Several selective 5-HT3 antagonists, including dolasetron (Anzemet), granisetron (Kytril), ondansetron (Zofran), tropisetron, and palonosetron, are available internationally. Multiple large, randomized clinical trials have shown no clinically significant difference among these drugs when used appropriately, with the exception of palonosetron, which demonstrates a higher binding affinity at the receptor site.[8,9,23,24] Further studies have demonstrated that a single dose of a 5-HT3-receptor antagonist prior to chemotherapy has efficacy equivalent to a multiple-dosing regimen.[25-27] Optimal dosing for the serotonin antagonists is controversial, as it appears that higher doses are not advantageous.[28] For example, the majority of ondansetron trials have indicated that an 8-mg dose is as effective as the higher, more expensive dose of 32 mg.[29,30] In general, the side-effect profiles of 5-HT3 antagonists show an advantage over that of metoclopramide. Central nervous system effects, extrapyramidal reactions, and sedation are not observed with serotonin antagonists; this is particularly beneficial in younger patients.[1] Common side effects of 5-HT3 antagonists include mild headache, transient transaminase elevations, and mild constipation with some agents.[1]

• Corticosteroids—Corticosteroids constitute another of the more active antiemetic choices. The most studied example is dexamethasone in oral and parenteral form. This is an expensive agent, and the best dose has not been established, but a single dose of 10 to 20 mg appears to be adequate. Caution is warranted in the clinical setting of diabetes, steroid myopathy, or other instances where steroid intolerance may exist. However, the short recommended course makes a corticosteroid a safe and easy option to offer patients with CINV. For prevention of delayed emesis, adequate doses of corticosteroids are viewed as advantageous when combined with metoclopramide [1]. The addition of a corticosteroid to 5-HT3 antagonists greatly improves antiemetic efficacy with
each agent. This effect is seen with cisplatin as well as with anthracyclines, cyclophosphamide, and carboplatin. Therefore, unless a clearly documented reason for not using such an agent has been demonstrated in a particular patient, a corticosteroid should be added whenever the emetic source is thought to warrant a serotonin antagonist [1].

**Less Active Antiemetics**

Antiemetics of lower activity levels include more classic agents such as phenothiazines, butyrophenones, and cannabinoids, all of which have some degree of antiemetic efficacy but greater side effects. When given intravenously, phenothiazines appear to be more active than by other routes but are associated with orthostatic hypotension. For this reason, phenothiazines are not highly recommended for the management of CINV, especially in the elderly. Oral forms of all three of these types of agents exhibit only modest activity and are of a similarly low efficacy. [1]

Semisynthetic cannabinoids such as nabilone and levonantradol, the active agent in marijuana (tetrahydrocannabinol, or delta 9-THC), and inhaled marijuana all appear to be of low and equal efficacy, with frequent autonomic side effects. Toxicities include dry mouth, hypotension, and dizziness. Dronabinol (Marinol) may be useful as an adjuvant to other antiemetics. [1] Antianxiety agents such as benzodiazepines have little efficacy as single agents, but seem to work well as adjuncts to antiemetics. They are especially useful as antiemetic adjuncts in patients receiving chemotherapy, which can be a stressful and emotionally charged setting. These drugs may be useful when given to patients with anticipatory emesis, starting one or more days before the next chemotherapy dose. Recommended oral or intravenous doses for lorazepam range from 0.5 to 1.5 mg. Side effects mainly include sedation, especially if the medication is given intravenously. [1]

**New Antiemetics**

**TABLE 4**

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<thead>
<tr>
<th>Schedule</th>
<th>Aprepitant (mg)</th>
<th>Placebo (mg)</th>
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</thead>
<tbody>
<tr>
<td>Day 1</td>
<td>100</td>
<td>0</td>
</tr>
<tr>
<td>Day 2</td>
<td>50</td>
<td>0</td>
</tr>
<tr>
<td>Day 3</td>
<td>50</td>
<td>0</td>
</tr>
</tbody>
</table>

Aprepitant Dosing for High-Risk Chemotherapy

**• Aprepitant**—Aprepitant is the first in a new class of antiemetics to be approved for prevention of acute and delayed nausea and vomiting—the NK-1-receptor antagonists. Investigators have identified substance P, an 11-amino acid neuropeptide found in the GI tract and central nervous system that has been shown to elicit vomiting in animal models. [1] Substance P binds to the neuroreceptor NK-1, and blocking this receptor has been linked to such clinical activity as depression, bladder irritability, inflammatory bowel disease, asthma, and functional GI diseases. NK-1 blockers also demonstrate a wide spectrum of antiemetic activity against numerous emetic stimuli. The combination of aprepitant with a 5HT-3 antagonist and a corticosteroid was evaluated in two large, randomized, double-blinded clinical trials with patients receiving high-dose cisplatin. [31] These studies found that the addition of aprepitant standard therapy produced a statistically significant increase in emesis control in both the acute and delayed phases, compared to standard therapy alone. [1] The most commonly observed side effects of aprepitant are mild and include fatigue, hiccups, constipation, anorexia, and headache (Table 4). [1,13,32]

**• Palonosetron**—A second new agent, palonosetron, is the first 5-HT3-receptor antagonist to be FDA-approved for the prevention of acute and delayed CINV. Compared to older 5-HT3 receptor antagonists (ie, ondansetron and dolasetron), palonosetron has demonstrated better prevention of both acute and delayed CINV, perhaps due to its higher serotonin- receptor binding affinity (30- to 100-fold) and prolonged half-life (~40 hours). [24] Palonosetron at 0.25 mg IV is indicated for the prevention of acute CINV associated with initial and repeat cycles of moderately and highly emetogenic chemotherapy and for prevention of delayed CINV associated with initial and repeated courses of moderately emetogenic chemotherapy. [24] Adverse reactions to palonosetron are similar to that of the other 5-HT3-receptor antagonists (headache, constipation, diarrhea, dizziness, and fatigue).

**Drug Treatment Guidelines**

**TABLE 5**
TABLE 6
Guidelines for Antiemetic Dosing Based on Phase of Emesis

With so many possible combinations of antiemetic drugs, not to mention the possible vast array of chemotherapeutic cocktails, how is one to navigate the best course in order to appropriately prevent CINV? In an attempt to simplify currently published antiemetic recommendations, a set of dynamic and evolving guidelines have been constructed (Tables 5 and 6).[1,13]

Nonmedication Treatment Adjuncts

In addition to standardized pharmacologic approaches to CINV prevention and treatment, now more than ever, our patients have access to a multitude of nonpharmacologic options. Once considered taboo and unsubstantiated, these modalities are undeniably accessible to our patients and for some are valuable adjuvants that complement pharmacologic therapy with the shared goal of improved quality of life. In general, these complementary therapies for nausea and vomiting can be divided into those supporting a patient's body, mind, and/or spirit.[33] More physical approaches include osteopathic manipulation,[15] chiropractic treatment, massage therapy, and yoga. Psychological, bioenergetic, or spiritual options with which a patient may find improved control of CINV include such modalities as hypnosis, biofeedback, guided imagery, reiki therapy, relaxation therapy, cognitive therapy, music therapy, and prayer.[34] Some oncology centers offer mind/body approaches as adjuvants to reduce nausea.[35] Both acupuncture and acupressure for CINV have been studied in multiple clinical trials. A recent pediatric study from Croatia (N = 120) demonstrated no statistically significant difference between laser acupuncture and metocloication in the occurrence and timing of postoperative nausea and vomiting (P < .001).[36-38] In another study, acupressure showed greater control in decreasing nausea when used as an adjunct to antiemetics (N = 739).[36,37]

Hope for the Future
For the patient facing the possibility of chemotherapy-related nausea and vomiting, the future is hopeful. With the trend toward increased knowledge and understanding of the pathophysiology of emesis, new antiemetic agents, a focus on prevention, and an openness to complementary adjuvants for symptom control, the future of the CINV guideline recommendations will continue to evolve. As clinicians, our goal is to provide patients with state-of-the-art therapy to prevent chemotherapy-induced emesis. This will be accomplished through the development of practical, user-friendly guidelines and an awareness of the complementary adjuvant options that are readily accessible. Until all patients are able to achieve complete control of chemotherapy-related nausea and vomiting, the search for new mechanisms, new agents, and improved quality of life will continue.

Financial Disclosure: The authors have no significant financial interest or other relationship with the manufacturers of any products or providers of any service mentioned in this article.

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Links: