

Non-infectious Supportive Care Issues in Patients with Hematologic Malignancies

Tumor lysis syndrome and gastrointestinal toxicities

by Amber P. Lawson, PharmD, BCOP

Hematologic malignancies present a unique challenge for clinicians with regards to disease management and supportive care. Although these malignancies do not constitute the majority of cancers diagnosed on a yearly basis, the recognition of predictable supportive care issues surrounding the diagnosis and treatment of hematologic malignancies is essential to reducing morbidities associated with the diagnosis and treatment of these diseases. According to the American Cancer Society, over 130,000 Americans will be diagnosed in 2008 with a hematologic malignancy in the form of leukemia, lymphoma, or multiple myeloma; additionally, 46,000 deaths in 2008 will be attributed to hematologic malignancies.¹ Patients diagnosed with hematologic

cancer may present specific challenges to clinicians in the area of supportive care due to both the underlying pathophysiology of the disease and the potentially curative treatment regimen the patient will receive. Pharmacists may play an integral role in the identification and management of supportive care issues in patients with hematologic malignancies by anticipating such issues and recommending appropriate measures for medication management.

TUMOR LYSIS SYNDROME

Tumor lysis syndrome is an oncologic emergency characterized by severe electrolyte disturbances that may ultimately lead to acute renal failure, seizures, cardiac arrhythmias or death. The destruction of rapidly proliferating malignant cells by chemotherapy or radiation therapy is the inciting event for tumor lysis syndrome.

This phenomenon may occur in patients with any hematologic malignancy, but those patients with a high tumor burden yet highly chemotherapy sensitive tumors are at increased risk. As the malignant cells succumb to chemotherapy, the release of intracellular contents into the bloodstream occurs so rapidly that increases in potassium, phosphorus and uric acid may be seen within six to 24 hours after chemotherapy treatment is initiated. Hypocalcemia may



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result secondary to hyperphosphatemia as the bloodstream pH promotes the binding of calcium and phosphorus in the form of calcium phosphate, which may precipitate into soft tissues.

The breakdown of nucleic acids following the lysis of malignant cells results in the formation of hypoxanthine and xanthine, respectively. Oxidation of xanthine by the enzyme xanthine oxidase then converts xanthine to uric acid. Uric acid is excreted via the kidney; although uric acid possesses a low solubility of 15 mg/dL at a lower pH like the acidic environment found in the distal tubules and collecting ducts of nephrons. Due to this low solubility, uric acid is more likely to precipitate in the distal tubules and collecting ducts as urate crystals. This physical obstruction causes increases in renal vasculature resistance and decreased renal blood flow which may lead to oliguric or anuric renal failure.

Tumor lysis syndrome may be further divided into laboratory tumor lysis syndrome (LTLS) and clinical tumor lysis syndrome (CTLS). Cairo and Bishop define laboratory tumor lysis syndrome as at least a 25% increase in two serum laboratory values of potassium, phosphorus, uric acid, or calcium beginning three days before or seven days after receiving cytotoxic therapy.² In order to satisfy criteria for clinical tumor lysis syndrome, the criteria for laboratory tumor lysis syndrome must be met plus one clinical complication of seizure, renal failure, cardiac arrhythmia, or sudden death. Specific risk factors for developing LTLS and potentially CTLS include a large tumor burden with a high proliferation rate, tumor chemosensitivity, and baseline high lactate dehydrogenase

Goal. The supportive care management of patients diagnosed with hematologic malignancies is often predictable and issues may be anticipated if the clinician is knowledgeable of these challenges. The goal of this program is to introduce pharmacists to complications associated with the diagnosis and treatment of these malignancies in order to facilitate prompt and effective resolution of these issues in order to achieve optimal patient outcomes.

Objectives. 1) Identify common toxicities of chemotherapy regimens employed in the treatment of hematologic malignancies; 2) Anticipate supportive care needs based on patient-specific characteristics and toxicities related to chemotherapy regimens; 3) Devise a monitoring plan to evaluate supportive care plans and to optimize medication-related outcomes; 4) Utilize and interpret current clinical oncology guidelines in the formulation of supportive care strategies for patients with hematologic malignancies

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(LDH) levels. Other patient-specific risk factors include pre-existing hyperuricemia or renal insufficiency. Specific hematologic malignancies that are at particularly high risk for contributing to the development of tumor lysis syndrome include Burkitt's lymphoma, acute lymphoblastic leukemia with white blood cell (WBC) counts greater than or equal to 100,000 cells/mm³, acute myeloid leukemia (AML) with WBC counts greater than or equal to 50,000 cells/mm³, and AML of monoclonal origin.³

The electrolytes affected by potential tumor lysis syndrome should be monitored frequently (i.e., multiple times per day) during induction chemotherapy. Established measures to prevent sequelae from hyperkalemia and hyperphosphatemia should be employed as necessary. The potential for hypocalcemia should also be monitored but judiciously treated since the administration of calcium may facilitate precipitation of calcium phosphate in the presence of hyperphosphatemia. The potentially severe morbidities associated with electrolyte disturbances should be carefully assessed and include cardiac arrhythmias, seizures, acute renal failure, and death.

Prevention of the deleterious effects of tumor lysis syndrome is the optimal management of potential complications due to this phenomenon. Intravenous hydration (2-3 L/m²/day) and diuresis remains the cornerstone of TLS prevention due to increased intravascular volume and hence increased renal blood flow and glomerular filtration. In an animal model, increasing urine flow rate was the only factor associated with prevention of urate-induced obstructive nephropathy.⁴ Patient-specific risk factors may preclude aggressive hydration without diuresis; each patient must be evaluated accordingly although diuresis is contraindicated in patients with obstructive nephropathies.

Uric acid possesses a urine solubility of 5 mg/dL at a pH of 5.0 while demonstrating a solubility of 200 mg/dL at a pH of 7.0. Therefore, historical management of TLS prevention has involved urinary alkalization in order to achieve maximal uric acid solubility in the urine. However, no clinical trial to date has demonstrated that urinary alkalization has decreased renal

morbidities and overall mortality related to clinical tumor lysis syndrome. Furthermore, urinary alkalization has no effect on hypoxanthine and xanthine solubility, and these precursors of uric acid may precipitate in the renal tubules as well with concurrent allopurinol treatment. Urinary alkalization is usually achieved through the intravenous administration of crystalloid fluids containing sodium bicarbonate, and the risk of inducing a metabolic alkalosis also exists. In addition, calcium phosphate is less soluble at an alkaline pH, and may precipitate in the presence of alkaline urine in the setting of hyperphosphatemia. Since the potential benefits of urinary alkalization are, at best, unclear compared to the possible harmful iatrogenic effects, urinary alkalization is not currently recommended in recently published guidelines regarding TLS prevention from the American Society of Clinical Oncology.³

In addition to hydration, other measures aimed at the reduction of uric acid are available for the prevention of tumor lysis syndrome. Allopurinol was introduced in 1965 and proved to be effective at lowering the formation of uric acid and also decreasing the risk of developing urate-induced nephropathy. An analog of xanthine, allopurinol acts as a competitive inhibitor of the enzyme xanthine oxidase, which converts purine metabolites into uric acid. However, when allopurinol blocks the formation of uric acid, the resulting accumulation of purine metabolites xanthine and hypoxanthine may also contribute to obstructive uropathies as mentioned above. It is important to note that allopurinol will inhibit the formation of uric acid but has no effect on existing uric acid concentrations; the peak effects of inhibition of uric acid formation may not be observed for several days. Allopurinol is generally well tolerated by most patients, with hypersensitivity reactions and fever among the most observed adverse effects. Allopurinol must be monitored with regards to drug interactions as well. Allopurinol has been shown to decrease clearance of other purine-based chemotherapeutic agents such as 6-mercaptopurine and azathioprine, among others.⁵

The enzyme urate oxidase converts existing uric acid to the more soluble al-

lantoin at an acidic pH, but the gene that encodes for this enzyme is not constitutively expressed in humans. Recombinant urate oxidase (commercially known as rasburicase) is a product of a gene cloned from *Aspergillus flavus* and expressed in a modified strain of *Saccharomyces cerevisiae*, which reduces the risk of allergic reactions. The utility of rasburicase in the prevention of tumor lysis syndrome is linked to the oxidation of uric acid to allantoin by the recombinant urate oxidase enzyme. The resulting rapid reduction in serum uric acid concentrations is achieved in anticipation of induction chemotherapy to be administered at least four hours after rasburicase administration and within 24 hours after administration of rasburicase.⁶ Notably, allantoin has five to ten times the solubility of uric acid in the acidic urine environment. Due to the urinary excretion of allantoin as opposed to uric acid, the use of intravenous fluids aimed at alkalizing the urine is not recommended in order to promote more efficient phosphorus excretion; an alkalized urine does not facilitate increased excretion of allantoin. While monitoring uric acid concentrations after rasburicase administration, uric acid samples must be placed in an ice water bath and tested promptly after collection in order to prevent false lowering of uric acid concentration due to the *ex vivo* activity of urate oxidase.

Rasburicase was approved by the Food and Drug Administration (FDA) in 2002 for the initial management of plasma uric acid levels in pediatric patients with leukemia, lymphoma, and solid tumor malignancies who are receiving anti-cancer therapy expected to result in tumor lysis and subsequent elevation of plasma uric acid. The approval was based in part on the results of a clinical trial involving the pediatric population. This multicenter randomized trial compared allopurinol to rasburicase in fifty-two pediatric patients with leukemia or lymphoma at high risk for tumor lysis. Patients received the assigned uric acid-lowering agent for five to seven days during induction chemotherapy. The primary efficacy end point was to compare the area under the serial plasma uric acid concentration curves during the first 96 hours of therapy. Four hours after the first dose, patients randomized to ras-

buricase compared to allopurinol achieved an 86% versus 12% reduction ($p < 0.0001$) of initial plasma uric acid levels.⁷ The authors concluded that rasburicase was a safe and effective alternative to allopurinol during initial chemotherapy. The study, however, was not powered to detect any differences between the groups with regard to incidence of renal failure or outcomes associated with renal failure.

The FDA-approved dose for rasburicase is 0.15 mg/kg or 0.2 mg/kg given intravenously once daily for five days. Due to the medication's high cost, several clinicians have pursued alternative dosing strategies such as the single dose administration of rasburicase, both as a weight-based dose and also a flat dose of the agent.⁸⁻¹⁰ Although re-dosing was necessary for few patients, the overall goal of lowering initial uric acid concentrations prior to chemotherapy was achieved. However, these strategies are not currently FDA-approved doses. Rasburicase should not be administered to patients with glucose-6-phosphate dehydrogenase (G6PD) deficiency since administration of rasburicase in affected individuals may result in hemolysis. Severe hypersensitivity reactions and methemoglobinemia may also occur with rasburicase administration.

Although tumor lysis syndrome may occur in certain patients with solid tumors receiving chemotherapy, this syndrome is characteristic of the clinical presentation and treatment of many hematologic malignancies. Careful monitoring and normalization of electrolytes and prompt institution of intravenous hydration and diuresis to maintain high urine output are the cornerstones of clinical management in order to avoid potential adverse outcomes. By identifying patients at high risk, pharmacists are able to assist in formulating a plan for clinical management and monitoring of these patients in order to facilitate the treatment of the patient's underlying disease.

GASTROINTESTINAL TOXICITIES

In the treatment of hematologic malignancies, combination chemotherapy regimens are often employed in order to achieve complete remission. Although this approach provides a better possibility of controlling the disease compared to single

agent chemotherapy in many cases, the potential for overlapping toxicities is also a concern. Among these expected toxicities are the effects of chemotherapy on the gastrointestinal tract. Gastrointestinal toxicities afflicting patients undergoing treatment for hematologic malignancies include nausea and vomiting, diarrhea, and mucositis.

Chemotherapy-induced nausea and vomiting (CINV) rank among the most feared adverse effects of chemotherapy treatment in many patient surveys over the past few decades; in fact, failure to control this menacing adverse effect may lead to patients delaying or refusing chemotherapy.¹¹ Although the psychological effects of CINV should not be overlooked, the physiological aspects of CINV may progress to life-threatening complications such as weakness, dehydration, severe electrolyte imbalances as well as physiological complications such as esophageal tears. Specific risk factors that predispose certain patients to CINV include female gender; very young or very old age; history of motion sickness, anxiety, or pregnancy-induced emesis, among other risk factors.¹²

When it comes to potential for inducing nausea and vomiting due to chemotherapy, not all chemotherapy agents are created equal. Alkylating agents such as cisplatin or carboplatin represent agents that are considered "high emetic risk," which means that without adequate pretreatment with antiemetics, greater than ninety percent of patients who receive

these agents would experience emesis. On the other hand, other antineoplastics are rated as "minimal emetic risk," which translates into less than ten percent of patients experiencing emesis after chemotherapy administration. Antiemetic regimens should be planned around the emetogenicity of the chemotherapy regimen. Since most chemotherapy regimens used to treat hematologic malignancies often combine different chemotherapeutic agents with differing mechanisms of action in order to achieve optimal disease control, the simultaneous administration of these agents will lead to higher emetogenic risk. It is important to note that there are a variety of mechanisms for inducing nausea, many of which remain unknown. Serotonin, dopamine, and neurokinin-1 are often implicated in the pathogenesis of CINV, but other mechanisms involving histamine and muscarinic receptors in the vestibular region may affect those who suffer from motion-related nausea and vomiting following the administration of chemotherapy.

Nausea and vomiting caused by chemotherapy has been described in the literature as occurring in at least three different pathophysiological and chronological phases; these distinctions are known as the anticipatory phase, the acute phase, and the delayed phase.¹³ As its name implies, anticipatory nausea or vomiting may occur as a learned response to prior experiences with chemotherapy based on sensory cues. For example, some patients describe that even the sight of the medica-

TABLE 1. DOSING OF SEROTONIN 5-HT₃ RECEPTOR ANTAGONISTS FOR PREVENTION OF CHEMOTHERAPY-INDUCED NAUSEA AND VOMITING

ANTIEMETIC	HALF-LIFE	SINGLE DOSE BEFORE CHEMOTHERAPY
Dolasetron (Anzemet®)	7 h	Oral: 100 mg IV: 100 mg or 1.8 mg/kg
Granisetron (Kytril®)	8.5 h	Oral: 2 mg IV: 1 mg or 0.01 mg/kg
Ondansetron (Zofran®)	4 h	Oral: 24 mg IV: 8 mg or 0.15 mg/kg
Palonosetron (Aloxi®)	40 h	IV: 0.25 mg

tion may precipitate nausea. Originating in the cerebral cortex, the most effective strategy for alleviating anticipatory CINV to date has been found to be relaxation techniques and premedication with anxiolytics such as lorazepam. The acute phase of CINV begins with the administration of chemotherapy and ends roughly 24 hours after administration of chemotherapy. The pathophysiology of acute CINV likely involves both central and peripheral mechanisms. The chemotherapeutic agent stimulates the chemoreceptor trigger zone in the central nervous system which exists just outside the blood brain barrier; the vomiting center is then activated through a release of a variety of neurotransmitters including serotonin, dopamine, and neurokinin-1 from the chemoreceptor trigger zone. Furthermore, the chemotherapeutic agent irritates the gastrointestinal mucosa, stimulating the release of neurotransmitters such as serotonin and neurokinin-1, which may further contribute to chemotherapy-induced nausea and vomiting. The delayed phase of CINV is defined as the period occurring at least 24 hours after the administration of chemotherapy. Often associated with the administration of alkylating agents, the mechanism of delayed CINV is not completely understood but is thought to involve neurokinin-1 receptors. The role of serotonin in the delayed phase of CINV has been demonstrated to be minimal to nonexistent compared to the acute phase.

The prevention of CINV in the acute phase has improved dramatically since the introduction of serotonin 5-HT₃ receptor antagonists in the 1990s. These agents primarily have the greatest impact in the acute phase, as many studies have demonstrated that serotonin-related nausea and vomiting events occur within the first 24 hours following chemotherapy administration. The current antiemetic guidelines from the American Society of Clinical Oncology consider all serotonin 5-HT₃ receptor antagonists equivalent in terms of efficacy and state that oral therapy is equivalent to intravenous therapy (Table 1).¹³ These agents are often co-administered with a steroid such as dexamethasone which proves to be more effective in preventing CINV than the administration of serotonin 5-HT₃ receptor antagonists

alone. The mechanism of action of steroids in this scenario remains unknown but is thought to be as a result of decreased prostaglandin production. For patients receiving high emetic risk regimens, both acute and delayed nausea and vomiting become a concern. Aprepitant is recommended to be added to a serotonin 5-HT₃ receptor antagonist and dexamethasone. The dose of aprepitant is 125 mg orally on day one, then 80 mg daily on days two and three, with dexamethasone given on days 1 through 4 and the serotonin 5-HT₃ receptor antagonist given on day one. For moderately emetogenic regimens (causing nausea and/or vomiting in 30-90% of patients), the guidelines state that the addition of aprepitant should be considered, but is not universally recommended due to lack of published efficacy data on multiple chemotherapy regimens that are moderately emetogenic. For chemotherapy regimens with low emetogenicity (causing nausea and/or vomiting in 10-30% of patients), single agent prophylaxis with dexamethasone, prochlorperazine, or metoclopramide is appropriate. In patients with a minimal risk of nausea or vomiting, defined as <10% chance of nausea or emesis, no routine prophylaxis has been recommended. Most chemotherapy regimens for the treatment of hematologic malignancies pose moderate to high emetogenic risk to patients. Of course, prevention of nausea and emesis is more effective than treatment. Break-through nausea should be treated with an agent of a different class. Agents that may be employed in the treatment of emesis include metoclopramide, dexamethasone, prochlorperazine, scopolamine, diphenhydramine, lorazepam, haloperidol, or olanzapine. The strategy remains targeting neurotransmitter receptors known to be in the CINV development pathways.

Although not limited to the treatment of hematologic malignancies as an adverse effect, mucositis, which is an inflammatory process possibly affecting the entire gastrointestinal tract from mouth to anus, is a frequent complication of treatment of those patients affected with blood cancers. Many chemotherapy and radiation regimens used in the treatment of hematologic malignancies may induce mild to severe mucositis. Oral mucositis may affect

quality of life due to pain and may also be considered a risk factor for sepsis in neutropenic patients.¹⁴ Patients undergoing hematopoietic stem cell transplantation (HSCT) may experience more frequent and more severe mucositis compared to patients undergoing chemotherapy alone as part of initial treatment of disease. The pathogenesis of this adverse effect has been further elucidated in the past five to ten years which may allow further advancements in the prevention and treatment of mucositis in patients with hematologic cancers.

The initiating event that triggers the development of mucositis appears to be the generation of reactive oxygen species (ROS) either by chemotherapy agents or radiation which, in turn, damage tissues and the epithelial cells of the vasculature that exist throughout the gastrointestinal tract, particularly in the oral cavity. Once the damage to the epithelial layer has occurred, the up-regulation of messenger signals leads to the production of inflammatory cytokines such as tumor necrosis factor alpha (TNF- α) or interleukin-1 (IL-1). This up-regulation of the inflammatory response subsequent to epithelial cell injury leads to recruitment of the immune system components such as macrophages that inflict further damage on the basal epithelium and submucosa. The ulcerative phase of mucositis may lead to bacterial colonization with gram-positive, gram-negative, and anaerobic organisms and pose an infectious risk to the patient as mucosal barriers and the immune system become further compromised. Cell wall components of bacteria will further recruit inflammatory cytokines and inflammation effects; patients may experience severe pain that is only controlled with intravenous narcotics as further inflammation affects the oral cavity. Patients usually experience clinical improvement upon leukocyte recovery as the healing process begins.¹⁵

Several grading systems for oral mucositis exist throughout the oncology community; the World Health Organization progressively grades mucositis from mild erythema (grade 1) to requiring parenteral nutrition (grade 4) to death (grade 5).¹⁶ Other grading systems such as those originating from the National Cancer

Institute (NCI) use the implementation of prophylactic intubation for airway protection as a measure of the ultimate consequence of mucositis in the surviving patient.¹⁷ Anticipation of the degree of mucositis expected in each individual patient due to patient-specific factors and the chemotherapy regimen may aid clinicians in minimizing risk of sequelae due to this complication. Promotion of good oral hygiene may decrease the number of oral ulcerations and subsequent pain; soft bristle toothbrushes and non-alcohol containing mouth rinses may promote good oral hygiene in this population. Smoking cessation is encouraged in order to avoid further exacerbation of inflammatory effects and worsening of ulcerations and pain.

Other measures may be employed in the prevention and treatment of mucositis as well, particularly in the setting of hematopoietic stem cell transplantation. Cryotherapy with ice chips for one hour has been shown to decrease the incidence of severe oral mucositis if administered at the time of high dose melphalan administration.¹⁸ Palifermin is a keratinocytic growth factor that has been shown to decrease the incidence and duration of severe oral mucositis in patients with hematologic malignancies receiving myelotoxic therapy requiring hematopoietic stem cell support.¹⁹ The Multinational Association for Supportive Care in Cancer (MASCC) clinical practice guidelines recommend the use of palifermin in patients undergoing autologous stem cell transplantation with total body irradiation (TBI) administered as part of the preparative regimen. Palifermin is dosed at 60 micrograms per kilogram for three days prior to the preparative regimen and at the same dose for three days post transplantation; administering the agent within 24 hours of the preparative regimen may actually worsen mucositis, so timing of administration should be vigilantly monitored.²⁰ The use of mouthwashes with topical anesthetics may be employed but the patient should be assessed frequently for uncontrolled pain and may ultimately require narcotics administered via patient controlled analgesia. The use of systemic glutamine, pentoxifylline, or mouthwashes containing chlorhexidine or granulocyte-macro-

phage-colony stimulating factor (GM-CSF) are not currently recommended by the guidelines; patients with severe mucositis may require the administration of systemic steroids in an effort to reduce the progression of the inflammatory event.²¹

DIARRHEA

Diarrhea is a frequent complication of chemotherapy treatment due to mitotic arrest of intestinal crypt cells as a consequence of chemotherapy administration leading to a decrease in absorptive surface area in the GI tract. After infectious causes have been excluded, the administration of antidiarrheals such as loperamide may prove beneficial in controlling diarrhea. Maintaining adequate fluid balance is essential in cases of severe diarrhea in order to avoid dehydration and severe electrolyte disturbances. Patients who have undergone allogeneic HSCT with an increase in stools should be evaluated for graft-versus-host disease. These patients often have diarrhea in excess of 1.5 liters per day occurring at least one month or later after the administration of high dose chemotherapy, may be uncontrolled with antidiarrheals and may ultimately require treatment with intravenous steroids. If patients have uncontrolled diarrhea with the administration of maximum doses of loperamide, octreotide may be administered in an attempt to control high-volume stools. Finally, many patients experience transient lactose intolerance after the administration of high dose chemotherapy, so a lactose-free diet may be considered to reduce the incidence of morbidity during periods of gastrointestinal toxicities.

CONCLUSION

Sequelae related to the diagnosis and management of hematologic malignancies are often predictable and the preemptive management of these supportive care issues may be anticipated. Medical professionals, including pharmacists, who are knowledgeable in the area of hematologic malignancies may play a vital role in the prevention, treatment, and monitoring of non-infectious complications in this setting. ●

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SELF ASSESSMENT QUESTIONS

Non-infectious Supportive Care Issues in Patients with Hematologic Malignancies

1. Patients at highest risk for tumor lysis syndrome include all of the following except:
 - a. Burkitt's lymphoma
 - b. Acute lymphoblastic leukemia with WBC $\geq 100,000$
 - c. Acute myeloid leukemia (non-monoblastic) with WBC $< 10,000$
 - d. All of the above are high risk populations
2. All of the following are acute electrolyte abnormalities in tumor lysis syndrome except:
 - a. Hyperphosphatemia
 - b. Hypercalcemia
 - c. Hyperkalemia
 - d. Hyperuricemia
3. Urinary alkalization facilitates the excretion of uric acid and is recommended by the ASCO clinical guidelines as a mode of prevention of morbidity associated with tumor lysis syndrome.
 - a. True
 - b. False
4. Which of the following dosing strategies have been documented in the literature regarding the dosing of rasburicase?
 - a. 0.15 mg/kg IV daily x 5 days
 - b. 0.2 mg/kg IV daily x 5 days
 - c. 0.15 mg/kg IV x 1 dose
 - d. All of the above
5. Which of the following compounds is most soluble in the urine?
 - a. Xanthine
 - b. Hypoxanthine
 - c. Uric acid
 - d. Allantoin
6. What percentage of patients receiving chemotherapy deemed to have a high emetogenic potential will experience nausea and emesis with no preventive antiemetics?
 - a. 75%
 - b. 80%
 - c. 85%
 - d. 90%
7. 5-HT₃ (serotonin) receptor antagonists are highly effective in the management of delayed nausea and vomiting in patients receiving chemotherapy for hematologic malignancies.
 - a. True
 - b. False
8. According to ASCO guidelines, which of the following regimens is considered most appropriate for the prevention of nausea and emesis in patients receiving highly emetogenic chemotherapy regimens in the non-transplant setting?
 - a. Aprepitant 125 mg on day 1, serotonin receptor antagonist on day 1, dexamethasone 12 mg on day 1 followed by aprepitant 80 mg on days 2 and 3 with dexamethasone 8 mg on days 2-4
 - b. Aprepitant 125 mg x 1 dose, serotonin receptor antagonist x 1 dose, and dexamethasone 12 mg x 1 dose, all on day 1
 - c. Serotonin receptor antagonist on day 1, dexamethasone 12 mg on day 1, followed by dexamethasone 8 mg daily on days 2-4
 - d. Serotonin receptor antagonist daily on days 1-4 with dexamethasone 8 mg daily on days 1-4
9. Which of the following drug classes is most effective in preventing anticipatory nausea?
 - a. Neurokinin-1 receptor antagonists
 - b. 5-HT₃ receptor antagonists
 - c. Benzodiazepines
 - d. Antihistamines
10. Scopolamine patches may be used in the treatment of chemotherapy-induced nausea thought to originate from the vestibular region of the central nervous system.
 - a. True
 - b. False
11. Which of the following preventive strategies regarding oral mucositis is not currently recommended?
 - a. Implementation of basic oral care
 - b. Cryotherapy
 - c. Smoking cessation
 - d. Administration of chlorhexidine mouth rinse
12. Palifermin should not be administered within 24 hours of cytotoxic chemotherapy in order to avoid worsening of mucositis.
 - a. True
 - b. False
13. Which of the following supportive care strategies should not be implemented in patients with severe mucositis?
 - a. Total parenteral nutrition
 - b. Systemic steroid administration
 - c. Pentoxifylline
 - d. Prophylactic intubation
14. Topical mouthwashes with anesthetics have been shown to effectively treat severe pain due to mucositis.
 - a. True
 - b. False
15. High-volume diarrhea that is refractory to loperamide may be treated with the following:
 - a. Octreotide
 - b. Intravenous hydration
 - c. Steroids if graft versus host disease is confirmed in allogeneic transplant patients
 - d. All of the above
16. How do you rate this lesson?
 - a. Very Good
 - b. Good
 - c. Poor
17. Did it meet the learning objectives?
 - a. Yes
 - b. No
18. How long did it take you to complete this lesson?



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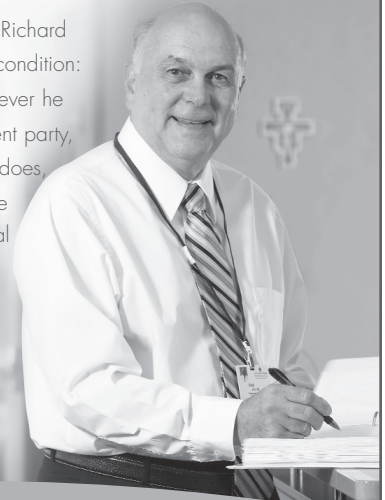
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