

Taming three high-risk chemotherapy



complications

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WHEN YOU CARE for adults undergoing chemotherapy for cancer, the drugs used to manage the disease can produce a wide range of adverse reactions and toxicities. Although individual chemotherapeutic drugs can cause specific complications, the risk increases when these drugs are administered in combination. If left untreated, some of these complications can be deadly.

This article reviews three common chemotherapy-associated complications that can be serious enough to require hospitalization: febrile neutropenia, chemotherapy-related nephrotoxicity, and chemotherapy-related enterotoxicity.

Febrile neutropenia

The most serious and potentially life-threatening complication of chemotherapy is febrile neutropenia, or the presence of fever in a patient with neutropenia. Febrile neutropenia is considered an emergency because even previously stable patients can quickly become hemodynamically unstable and critically ill. Prompt assessment and interventions are necessary to reduce morbidity and mortality.

According to recently updated guidelines from the Infectious Disease Society of America (IDSA), neutropenia is present when the patient's absolute neutrophil count (ANC) is less than 500 cells/mm³ or is anticipated to fall below this level in the next 2 days. An ANC under 100 cells/mm³ is often called "profound" neutropenia.¹ This level of neutropenia needs to be confirmed by a manual differential rather than an automated differential.

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In patients with a hematologic malignancy, even if the ANC is within the normal range, the neutrophils are dysfunctional and lack the normal ability to fight infection. The term “functional” neutropenia is used in this setting.¹ In all these situations, remember that the risk of infection increases the longer neutropenia persists and the lower the ANC count.

Fever is present when body temperature is 38.3° C or greater at one measurement, or 38° C or greater over 1 hour. By definition, temperature is taken orally and the febrile episode has no obvious etiology.²

The bone marrow produces red blood cells, white blood cells (WBCs), and platelets throughout life. WBCs, including neutrophils, are key components of the body's cellular immunity. Neutrophils are the first WBCs to rush to an infection site to guard against progressive infection. Chemotherapy, however, kills bone marrow cells in the reproductive phases, so fewer neutrophils are produced and replacing them takes time. This period of low cell counts, called the nadir, is when the patient is at greatest risk. Infection may result when the patient's remaining neutrophils fail to phagocytize and destroy microorganisms.

Vigilance is vital

When a patient undergoing chemotherapy develops a fever, nursing assessments and interventions are critical to a good outcome. Ask about current chemotherapy (dates, drugs, doses, frequency), any prior therapy for cancer, signs and symptoms of infection, and comorbidities. Also document vital signs, pulse oximetry values, and daily weights. Perform medication reconciliation.

If severe neutropenia is an expected adverse reaction to the prescribed chemotherapy regimen, your patient may have received a myeloid colony-stimulating factor (CSF) drug

(pegfilgrastim or filgrastim) to stimulate neutrophil production; if so, check the documented date(s) that the patient received the medication. CSFs aren't generally recommended to treat neutropenia and are most often prescribed prophylactically for patients at risk for developing febrile neutropenia.¹

Perform a complete physical assessment, including assessment of the lungs, gastrointestinal (GI), and genitourinary tracts; skin and mucous membranes; and venous access sites to look for signs and symptoms of infection.³ Keep in mind that fever may be the only sign of infection; local signs and symptoms of acute inflammation, such as pain, erythema, and edema may be absent due to neutropenia. However, in some patients who have difficulty mounting an immune response, fever may not be present and the patient may have a temperature below normal. Additional assessments required include pulmonary, cardiovascular, and neurologic status.⁴

Send specimens for lab work as prescribed. Tests typically include a complete blood cell count with differential and platelet count, serum electrolytes, and renal and liver function tests. Draw two sets of blood cultures (one obtained peripherally and the other from a central venous catheter, if present; otherwise, obtain specimens from two different peripheral sites). Obtain specimens for other cultures as indicated, depending on assessment findings.¹ Additional diagnostic studies are symptom-related, such as a chest X-ray for cough or urinalysis with culture if the practitioner suspects a urinary tract infection.³

Targeting treatment

Prompt initiation of therapy with prescribed I.V. fluid and broad-spectrum antibiotics administered within 60 minutes of the start of

the febrile episode lead to the best outcomes for a patient with febrile neutropenia.⁴ High-risk patients require hospitalization for treatment. Patients meeting low-risk criteria may receive outpatient oral or parenteral antibiotic therapy.¹

Monitor vital signs and pulse oximetry at least every 4 hours and more often as needed to evaluate the patient's response to treatment. Continue physical assessments at least once per shift and pay attention to any identified sites of infection, such as a central venous catheter site or the genitourinary tract if a urinary tract infection is diagnosed. However, many patients with cancer who develop febrile neutropenia don't have an identifiable source of infection, so the condition is considered fever of unknown origin.⁵

If an infection source is identified, your patient's antibiotic therapy will be modified to target the specific pathogen. The patient will continue receiving antibiotics depending on the identified source, the recovery of the neutrophil count to a non-neutropenic level, resolution of the fever, and the return of hemodynamic stability.

If the patient will continue I.V. antibiotic therapy after discharge, arrange for a consult with a home infusion practice. An infectious disease consultation may be indicated if the patient has a complicated disease process, such as acute leukemia with febrile neutropenia.

Your patient may have more than one febrile episode while neutropenic. If fever recurs, notify the health-care provider, who may prescribe additional cultures and diagnostic studies along with additional or different antibiotics. The longer the patient is neutropenic, the greater the risk of additional bacterial, fungal, and viral infections, so continue to monitor the patient closely. For many patients, febrile neutropenia

will result in treatment delays and also, in some patients, dose reductions.

While the patient is hospitalized, ensure optimal infection control practices.⁶ These include screening visitors for infectious diseases such as seasonal influenza.¹

Follow appropriate care bundles designed to minimize infection risk, such as the central line bundle recommended by the Institute for Healthcare Improvement (IHI), according to facility policy. A care bundle is a group of interventions that, when consistently applied together, significantly improves outcomes. The IHI's central line bundle includes hand hygiene, maximal barrier precautions, chlorhexidine skin antisepsis, optimal catheter site selection, daily review of line necessity, and prompt removal of unnecessary lines.⁷ Monitor the patient for development of antibiotic-associated diarrhea and send stool specimens to test for *Clostridium difficile* toxin as indicated.

The IDSA guidelines contain specific environmental precautions to reduce the risk of infection.¹

- Perform meticulous hand hygiene, which is the most effective method of reducing healthcare-associated infections.
- Follow standard barrier precautions.
- Utilize infection-specific isolation precautions for symptomatic patients.
- Place patients who've undergone a hematopoietic stem cell transplantation (HSCT) in a private room. Place patients who've undergone an allogeneic HSCT in a private room equipped to provide air exchange and high-efficiency particulate air (HEPA) filtration.
- Reduce patient exposure to pets and other animals, and plants, including cut or dried flowers, by keeping these out of the patient's room.

Promote your patient's comfort by administering antipyretics such as acetaminophen as prescribed. If the patient has chills, provide additional blankets and increase ambient temperature; small doses of I.V. meperidine may be prescribed to manage rigors.

Febrile illness is fatiguing, so your patient may need assistance with activities of daily living. Initiate safety precautions to reduce the risk of injury related to falls. Reassure the patient that he or she should begin to feel better as antibiotics combat the infection and the neutrophil count increases.

Educate any patient who's undergoing chemotherapy about the signs and symptoms of infection and the crucial need to immediately report any that develop to the healthcare provider. Make sure your patient understands that febrile neutropenia could result in a life-threatening illness and requires immediate medical intervention. Remind patients to keep up-to-date with appropriate vaccinations, such as an annual inactivated influenza vaccine, and to avoid exposure to people vaccinated with live vaccines. Tell them to ask their healthcare provider when they

Risk factors for chemotherapy-related nephrotoxicity^{8,16}

- fluid volume deficits
- advanced age
- preexisting renal dysfunction
- concomitant use of nonchemotherapeutic nephrotoxic drugs, such as NSAIDs, aminoglycosides, or iodinated contrast media
- comorbidities (such as diabetes)
- high drug dose
- urinary tract obstruction, such as obstruction secondary to tumor.

can safely be exposed to people who've received live vaccines.

Chemotherapy-related nephrotoxicity

Many chemotherapy drugs can cause renal problems by damaging the glomerulus, renal tubules, interstitium, or microvasculature. (See *Get to know drugs with nephrotoxic effects*.) Adverse reactions range from mild (an asymptomatic increase in serum creatinine) to potentially fatal (acute kidney injury). For factors that increase the risk of chemotherapy-related nephrotoxicity, see *Risk factors for chemotherapy-related nephrotoxicity*.

Acute kidney injury can be oliguric or nonoliguric and, in patients undergoing chemotherapy, may have prerenal, intrarenal, or postrenal causes. For examples, see *Exploring reasons for acute renal failure*.

Cisplatin is a commonly used nephrotoxic antineoplastic that can damage both the proximal and distal tubules. Injury is cumulative and dose-related.⁸

High-dose cisplatin therapy may cause acute tubular necrosis (ATN), restricting the tubules' ability to reabsorb water, sodium, magnesium, and other electrolytes and resulting in electrolyte abnormalities that may become chronic. Even when aggressive pre- and posthydration with

Get to know drugs with nephrotoxic effects^{16,17}

Alkylating agents

- carboplatin
- cisplatin
- cyclophosphamide
- ifosfamide
- melphalan
- oxaliplatin

Antimetabolites

- azacitidine
- gemcitabine
- methotrexate

Cytotoxic antibiotics

- mitomycin C

Vinca alkaloids

- vincristine.

mannitol-induced diuresis are part of the cisplatin regimen, the patient may develop nephrotoxicity, so continue to closely monitor renal function after drug administration.

Methotrexate affects the renal tubules and collecting ducts, and may cause ATN. High-dose therapy may trigger this type of injury when the drug precipitates out of solution and collects in the tubules and ducts. Acute kidney injury may occur at any time while the patient is actively receiving treatment.⁹ To reduce the risk of renal injury with high-dose therapy, patients undergo hydration with sodium bicarbonate-containing I.V. fluids to alkalize the urine (methotrexate is better eliminated in an alkaline urine environment). Urine pH testing starts during prehydration and continues postdrug administration until the body has eliminated the methotrexate. Methotrexate drug levels are closely monitored.

Clinical manifestations of nephrotoxicity

Patients who develop chemotherapy-related nephrotoxicity may be asymptomatic or have signs and symptoms of fluid volume excess or deficit (depending on the cause) and elec-

trolyte imbalances, including hypocalcemia and hyperkalemia.¹⁰ Nausea and vomiting may develop as metabolic waste products such as urea and creatinine accumulate.

Key blood work to help identify nephrotoxicity includes renal function tests. Abnormal results indicating nephrotoxicity include elevated serum creatinine, elevated blood urea nitrogen (BUN), elevated BUN/creatinine ratio, and decreased urine creatinine clearance. The patient may also have abnormal serum electrolyte levels. Urinalysis and urine electrolytes (such as sodium and potassium) also may shed light on kidney function.

Nursing interventions that focus on chemotherapy-related nephrotoxicity include obtaining the patient's history, performing a physical assessment, identifying risk factors for nephrotoxicity, and reviewing lab results. Pay attention to any potentially nephrotoxic medications that the patient has received recently or takes regularly, such as nonsteroidal anti-inflammatory drugs (NSAIDs) and drugs that can cause hyperkalemia (such as angiotensin-converting enzyme inhibitors and potassium-sparing diuretics, such as spironolac-

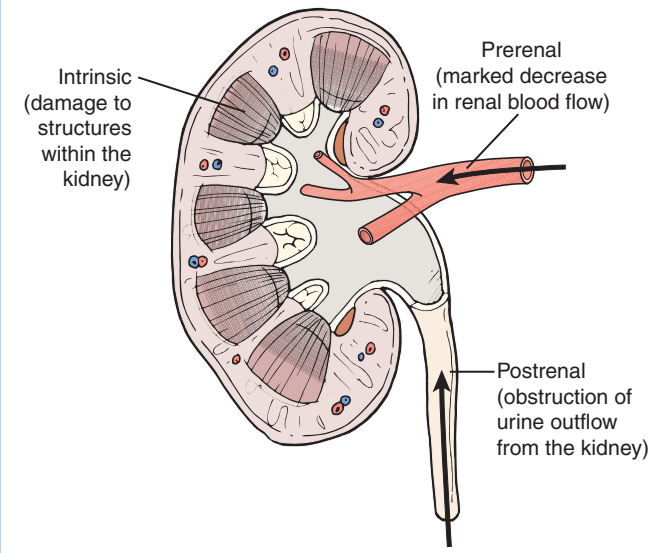
tone). These should be discontinued and replaced with similar, less nephrotoxic agents, as prescribed.

Many drugs are excreted by the kidneys, and impaired renal function can impair drug excretion, leading to prolonged circulating drug levels that are toxic to other organs. Assess the patient for signs and symptoms of drug toxicity.

Assess for signs and symptoms of fluid volume overload or deficit. (See *Recognizing fluid volume deficit and excess*.) Administer I.V. fluids as prescribed. Obtain your patient's daily weight and orthostatic vital signs, and compare your findings with prior assessments.

Renal assessment also includes accurate measurement of intake and output, and bladder palpation and/or ultrasound bladder scanning to assess for urinary retention. Determine the patient's usual voiding patterns before admission and assess for oliguria, polyuria, nocturia, hematuria, or flank pain.

Your patient's food plan may need to be modified to control intake of fluid, protein, and electrolytes. Consult a dietitian as needed. Closely monitor your patient's serum electrolyte levels and treat imbalances



The diagram illustrates a kidney with three labeled areas of concern: 1. **Prerenal** (marked decrease in renal blood flow): Indicated by a red arrow pointing to the renal artery entering the kidney. 2. **Intrinsic** (damage to structures within the kidney): Indicated by a red arrow pointing to the internal renal structures, specifically the nephrons. 3. **Postrenal** (obstruction of urine outflow from the kidney): Indicated by a red arrow pointing to the ureter, which is shown with a blockage.

Exploring reasons for acute renal failure^{18,19}

The causes of acute renal failure are commonly classified as prerenal, intrarenal or intrinsic, and postrenal.

Prerenal

- dehydration/fluid volume deficit
- hypotension
- NSAIDs
- sepsis

Intrarenal (intrinsic)

- electrolyte imbalances
- infection
- nephrotoxic medications, including antineoplastics
- preexisting renal damage
- tumor lysis syndrome

Postrenal

- bladder outlet obstruction
- bilateral ureteral obstruction.

as prescribed. Obtain 12-lead ECGs and institute continuous cardiac monitoring as indicated. If kidney function fails to improve with medical management or quickly deteriorates, the patient may require dialysis. If the patient requires additional chemotherapy, the chemotherapy regimen will require alteration to reduce the risk of worsening renal injury.

Chemotherapy-related enterotoxicity

Chemotherapy-associated toxicity affecting the GI tract is common and expected. Although often manageable, each of the following can be severe enough to require hospitalization.

- *Chemotherapy-induced nausea and vomiting (CINV)*. If frequent and severe, vomiting can cause a fluid volume deficit and electrolyte imbalances.
- *Mucositis* interferes with eating and drinking.
- *Diarrhea* causes loss of fluid and electrolytes (sodium, potassium, and bicarbonate) and irritates the perirectal skin.

CINV is the result of neurotransmitter production that stimulates the brain's emetic center.¹¹ Modern antiemetics such as the serotonin receptor antagonists and neurokinin-1 receptor antagonists administered in combination with corticosteroids have decreased the incidence and severity of *acute emesis* in patients undergoing chemotherapy. Unfortunately, uncontrolled nausea and emesis can result in patients developing anticipatory nausea and vomiting. (See *Factors affecting the risk of CINV*.)

Delayed emesis (emesis occurring more than 24 hours after treatment) poses more of a challenge. Regimens commonly associated with delayed emesis include highly emetogenic cisplatin.¹² Other drugs that cause delayed emesis include cyclophos-

Recognizing fluid volume deficit and excess

Fluid volume deficit

Acute weight loss (% of body weight)

- mild fluid volume deficit: 2%
- moderate fluid volume deficit: 5%
- severe fluid volume deficit: >8%

Decreased interstitial fluid volume

- decreased skin and tissue turgor
- dry mucous membranes
- sunken, soft eyeballs

Decreased vascular volume

- postural hypotension
- weak, rapid pulse
- decreased vein filling
- hypotension and shock (severe deficit)

Fluid volume excess

Acute weight gain (% of body weight)

- mild fluid volume excess: 2%
- moderate fluid volume excess: 5%
- severe fluid volume excess: >8%

Increased interstitial fluid volume

- edema

Increased vascular volume

- full, bounding pulse
- venous distention
- pulmonary edema (severe excess): shortness of breath, crackles, dyspnea, cough

Source: Porth CM. *Essentials of Pathophysiology*. 3rd ed. Philadelphia, PA: Lippincott Williams and Wilkins; 2011:173.

phamide, the anthracycline antibiotics doxorubicin and epirubicin, and the other platinum compounds (in addition to cisplatin), carboplatin and oxaliplatin.¹¹

Mucositis and diarrhea result from the direct effect of antineoplastic drugs on rapidly dividing cells in the GI tract. Ulcers or denuded areas may develop in the mouth and in the absorptive areas of the intestines. Oral ulcers are painful and interfere with the patient's ability to chew and swallow foods and fluids. Ulcers or denuded areas in the intestines reduce the absorptive surface area and interfere with water and chloride absorption, resulting in diarrhea.¹³ A number of chemotherapy agents, including irinotecan and 5-fluorouracil, can trigger diarrhea.

Fluids and electrolytes out of balance

When adverse GI reactions to chemotherapy are poorly controlled, fluid volume deficits and electrolyte imbalances result. Your patient assessment should include vital signs and daily weights, and a comparison with prior assessments to determine weight loss. If you note signs and symptoms of fluid volume deficit, assess orthostatic vital signs.

Ask what food or fluid the patient has been able to consume since receiving chemotherapy, including how much and how well it was tolerated. Also ask the patient to describe the onset, duration, frequency, amount, and characteristics of vomitus or diarrhea, and any self-care measures taken to control these reactions. Ask the patient to describe stool characteristics, including the presence of blood or mucus, and other changes in the stool or bowel habits. Evaluate any accompanying signs and symptoms, such as abdominal pain, distension, and flatus.

Ask the patient to remove any dental appliances and assess all mucous membrane surface areas, including lips, teeth, gums, hard and soft palates, and all tongue surfaces. Examine mucous membranes for moisture and color, and assess personal oral care or hygiene of the mouth (such as cleanliness of the mouth and other indications of how well the patient has cared for teeth and gums). Look for ulcers and signs of inflammation and infection.¹⁴

If your patient has oral ulcers, ask about their onset and associated signs and symptoms, such as dysphagia and odynophagia, gingival bleeding, and dental pain. Include a pain intensity

rating for any pain the patient is experiencing. Also determine if the patient has any removable dental appliances such as dentures. If dentures are irritating the oral mucosa, advise the patient to remove them until healing occurs. If dentures are loose or ill-fitting, instruct the patient not to use them until a dentist evaluates and corrects the underlying problem because they'll irritate the oral mucosa.

Perform an abdominal assessment, inspecting for symmetry and abnormalities, such as distension. Auscultate bowel sounds, and palpate for abdominal masses and other abnormalities. Assess the sacrococcygeal and perianal areas for abnormalities such as ulcers, inflammation, or excoriations from diarrhea. Evaluate skin turgor, keeping in mind that tenting isn't a reliable indicator of dehydration in older adults because of the loss of skin elasticity associated with aging.

Nursing interventions

A patient who's hospitalized with signs and symptoms of chemotherapy-related enterotoxicity (such as vomiting, diarrhea, and severe mucositis) that result in fluid and



Uncontrolled nausea and emesis can result in a patient developing anticipatory nausea and vomiting.

electrolyte imbalances requires I.V. hydration and electrolyte replacement. In addition, to manage **nausea and vomiting**, your patient should have nothing by mouth. Provide oral care after vomiting to remove gastric acids and promote comfort. Administer antiemetics as ordered, assess the patient's response to treatment, and monitor for adverse reactions to the antiemetic, such as dizziness, headache, sedation, or dysrhythmias associated with ondansetron administration.

After nausea and vomiting subside, the patient can slowly resume intake of broth, tea, crackers, and other bland foods and liquids. Once the patient can tolerate these items, slowly add other foods that aren't salty, fatty, or spicy. Avoid food with a strong odor. Consider using relaxation techniques and guided imagery to help the patient manage symptoms.¹⁵

Chemotherapy-induced diarrhea calls for immediate treatment with antidiarrheal medication as well as

dietary changes. The patient should consume only bland foods and avoid dairy products, spicy foods, alcohol, caffeine-containing products, foods high in fiber or fat, and some fruit juices, including orange juice.¹³ Encourage drinking 8 to 10 large glasses of clear liquids a day, eating frequent small meals, and choosing high-potassium foods such as bananas and potatoes. About 2 weeks after the diarrhea subsides, dairy products can usually be slowly reintroduced.

Useful antidiarrheal medications include loperamide and diphenoxylate hydrochloride with atropine sulfate. Following the package instructions for loperamide is appropriate unless the patient's chemotherapy regimen includes irinotecan; in that case, the healthcare provider will prescribe more aggressive dosing. Make sure your patient understands the need to adhere to the aggressive dosing schedule prescribed by the healthcare provider.

Oral care for **mucositis** includes oral rinses with a weak solution of salt and baking soda (one-half teaspoon of salt and one teaspoon of baking soda in a quart of water) every 4 hours to maintain oral hygiene and soothe the tissues. Some facilities use various formulations of topical analgesics to manage mucositis-associated pain, such as viscous xylocaine combined with diphenhydramine and an antacid (sometimes called "miracle mouthwash"), but no scientific evidence supports their effectiveness. To prevent adverse reactions such as sedation and oral injury caused by numbness, warn the patient not to swallow a xylocaine-based mix (unless otherwise prescribed) or to exceed the prescribed volume. When oral care and topical medications don't control the pain of mucositis, the healthcare provider may prescribe systemic medications, such as oral or parenteral opioids.

Factors affecting the risk of CINV²⁰

Various patient- and drug-related factors increase the risk of CINV, including:

- intrinsic emetogenicity of the chemotherapeutic agent, its route, rate of administration, and dose
- emesis with prior chemotherapy
- female gender
- younger age
- patients who are rapid metabolizers of certain serotonin receptor antagonists.

Patients who experience acute emesis are significantly more likely to have delayed emesis. Those with a significant history of alcohol use are less susceptible to CINV than those without such a history.

Oral hygiene and assessments are crucial. If the patient's pain is severe enough to interfere with oral care, provide analgesia beforehand as prescribed. Patient-controlled analgesia is an effective administration method in this situation.

Meticulous nursing care

Chemotherapy can trigger potentially life-threatening adverse reactions that may require hospital admission. Your meticulous assessments, interventions, and patient education can help protect your patient during the crisis and minimize the risk of future complications related to chemotherapy. ■

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