

Please note: The September 2004 ONS News and Oncology Nursing Forum mailing included a supplement titled *Spotlight on Symposia*. The incorrect sponsor was listed for the program "Demystifying CINV Control in the Complex Aging Patient: Assessing the Complexities of the Aging Oncology Patient." Please replace pages 5–8 in your copy of *Spotlight on Symposia* with these corrected and reprinted pages. To obtain additional copies of *Spotlight on Symposia*, please contact ONS Customer Service at 866-257-4667 or customer.service@ons.org.

Demystifying CINV Control in the Complex Aging Patient: Assessing the Complexities of the Aging Oncology Patient

Challenges of Older Patients

In older patients, the incidence of cancer and the use of aggressive and potentially emetogenic chemotherapy is on the rise. The most common risk factor for cancer is increasing age. Because individuals 85 years and older now make up the fastest growing segment of the United States population, according to the U.S. Census Bureau, an integrated approach to gerontology patients and cancer therapy must be considered.

Rita S. Wickham, PhD, RN, AOCN®, CHPN, explained that chronological age is not a reliable predictor of the extent of physiologic changes a patient undergoes. The Oncology Nursing Society and the Geriatric Oncology Consortium contend that measurements beyond chronology

must be considered, such as biologic, functional, and personal dimensions, because active older people living healthy lifestyles may be functionally younger than their chronological age.

"Conversely, morbidity or lifestyle may cause individuals to be functionally older than their chronological age," Wickham noted. Decreased musculoskeletal mass, functional limitations and multiple geriatric syndromes in the "oldest old"—those 85 years or older—often cause people to classify these individuals as frail. All of these variables can increase susceptibility to chemotherapeutic toxicities.

Changes in the liver and kidneys, fat-to-muscle ratio, and total body water occur with normal aging. The liver loses hepatocytes while concurrently developing fibrosis and increased fat. These changes are partly responsible for age-associated shrinkage of the liver by approximately 25%, as well as decreased hepatic blood flow. Cells in the renal cortex and parenchyma are lost and the kidneys shrink by some 20%, with an associated decline in renal blood flow. This results in decreased glomerular filtration rate (GFR) and creatinine clearance. Lastly, total body fat increases

Oncology nurses play a vital role in the management of chemotherapy-induced nausea and vomiting (CINV). Serotonin-receptor antagonists, neurokinin 1 antagonists, and steroids can control nausea and vomiting associated with cancer chemotherapy, improving patients' abilities to tolerate and complete the full course of cancer treatment. Safe and effective management of CINV in older patients involves special considerations, including comorbidities, potential for drug-drug interactions and toxicities, physiologic changes related to aging, and concomitant use of complementary and alternative therapies. In this session, a multidisciplinary group of oncology specialists discussed the nursing considerations related to conventional and complementary management of CINV in this patient population.

by 11%–16%, while total muscle mass and body water decrease. These changes may affect drug pharmacology.

The pharmacologic process has three phases: pharmaceutical, pharmacokinetic, and pharmacodynamic. The pharmaceutical phase involves the disintegration and dissolution of formulated drugs. Pharmacokinetics is what the body does to the drug and includes absorption, distribution, metabolism, and excretion. Pharmacodynamics is what the drug does to the body and relates to drug action at a receptor site.

"In the aging population, the changes in pharmacodynamics are not well characterized," Wickham said, adding that differences in receptor sensitivity and number, and/or enhanced expression of the multidrug resistance gene may occur. This accounts for much individuality of response to particular drugs. Changes in body water and body mass may alter drug distribution, affecting the drug's onset of action and elimination.

Reduced total body water often leads to higher blood and tissue concentrations.

Presenters

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Key Considerations With Older Patients

- Age is the number one risk factor for cancer.
- Older patients take more drugs than younger patients.
- Older patients typically have one or more comorbidities.
- Older patients take an average of 4–6 medications per day.
- Older patients often use over-the-counter drugs and complementary and alternative therapies.

A higher percentage of body fat leads to increased volume of distribution for lipophilic (fat-soluble) drugs and may increase their elimination half-lives, resulting in elevated drug levels.

Wickham explained that the liver is the chief organ of *metabolism* and plays a primary role in the elimination of many chemotherapeutic agents. As people age, the liver shrinks up to 25%, they experience loss of hepatocytes, and parenchyma is replaced by fibrosis and increased fat. The ability of the liver to metabolize drugs via the cytochrome P-450 system is decreased. The physiologic alterations of aging may significantly reduce presystemic (first-pass) metabolism.

Changes in the kidneys also affect pharmacokinetics. The kidneys are the primary organs of *excretion*. The effects of aging on the kidneys can result in delayed drug elimination, increased drug toxicity, altered acid-base balance and disturbed water homeostasis. Organ function can be further compromised by stress from disease, environmental factors and concomitant drug administration.

Metabolism and hepatic and renal effects are other potential mediating factors that affect how older people react to medications. Stress from disease, environment, and drugs can affect hepatic and renal systems.

Wickham explained that older people represent 13% of the population but take 25%–35% of all prescription drugs. Further, 61% of cancers in the United States occur in people 65 years or older. Older people are more likely to take over-the-counter drugs and nutraceuticals or complementary and alternative medicines (CAMs). One trial showed that 41% of older patients had used CAMs (e.g., herbs, multi- and megavitamins, dietary supplements) (Astin, Pelletier, Marie, & Haskell, 2000). Additionally, older people typically have one or more comorbidities such as cardiovascular disease, chronic obstructive pulmonary disease, diabetes mellitus, or renal dysfunction. Furthermore, patients 75 years or older are more likely to use more than four drugs, known as polypharmacy. Polypharmacy use increases with aging.

With the average older person taking 4–6 medications per day (Heft & Mariotti, 2002; Morris, Grossman, Barkdoll, Gordon, & Chun, 1987; Schmucker, 1984; Yancik & Ries, 2000). With new diagnoses, more drugs are added and patients with cancer take an even greater number of medications. The risks associated with polypharmacy include increased adverse drug reactions, drug-drug interactions, nonadherence, hospitalization, and medication errors. These risks are enhanced by multiple comorbidities (Karas, 1981). The physiologic changes of aging magnify the risks associated with polypharmacy by decreasing the therapeutic index of particular drugs and increasing the risk for drug interactions. Data show that older patients are twice as likely as younger patients to have adverse drug reactions. Additionally, the risk of drug-related deaths increases exponentially in accordance with the number of medications taken.

Wickham said that a rule of thumb for prescribing for older patients is that drugs tend to be *stronger* and *longer* in older patients. She recommended that nurses identify drugs not recommended for older individuals. Also, nurses should be able to distinguish between symptoms of adverse drug reactions and cancer manifestations. Sometimes these symptoms are nonspecific and overlapping. This is why collaboration between physicians, nurses, pharmacists, patients, and families is critical for the patient to get the best treatment, Wickham said.

Nursing Assessment

Regular nursing assessment of older patients with cancer is critical as well. In assessing physical health, Wickham said

nurses should check for general health, performance status, nutrition, fluid balance, and cognitive status. Socioeconomic factors also play a role. Nurses need to ask if a caregiver is at home, and if cost and payment issues are of concern. They should monitor how many prescription drugs the patient is taking, whether the drugs are all necessary and appropriate or if duplication of effort is occurring. Additionally, what over-the-counter medicines and CAMs are patients taking? Wickham noted that older people often view these drugs as natural and safer, but this cannot be assumed as no uniformly accepted definition of CAMs exists, and these products are not regulated. Complementary medicines can be used as an adjunct to medical treatment, often decreasing symptoms and increasing quality of life. However, nurses and patients need to work together to investigate these possibilities.

Wickham shared information about the Beers Criteria, which lists several drugs that are “inappropriate” for older patients. These include propoxyphene, pentazocine, muscle relaxants, meperidine, amitriptyline and many others.

Alternative medicines however, are promoted as anticancer treatment, and some patients use them instead of mainstream treatment. In reality, Wickham said, they can be biologically active, harmful, and costly. Therapies include Chinese medicine, homeopathy, and naturopathy. Mind-body interventions include relaxation, hypnosis, prayer, and music therapy. With all the possible therapies available, and in light

Beers Criteria: Inappropriate Drugs for Older Patients

- Propoxyphene
- Pentazocine
- Muscle relaxants
- Meperidine
- Amitriptyline
- Ferrous sulfate > 325 mg per day
- Trimethobenzamide
- Barbiturates (except for seizures)
- Ketorolac
- Mineral oil
- Amphetamines
- Clonidine
- Some nonsteroidal anti-inflammatory drugs
 - Naproxen
 - Piroxicam
 - Indomethacin

Note. Based on information from Fick et al., 2003

of the data that show that up to 41% of patients use CAM (Astin et al., 2000), Wickham said open, respectful discussions are vital to helping patients to identify potentially harmful measures.

Safe and Effective Therapy

CINV (chemotherapy-induced nausea and vomiting) is among the most devastating adverse effects of cancer treatment, significantly affecting quality of life. According to Susan Goodin, PharmD, BCOP, CINV is frequently rated as one of the most feared side effects of chemotherapy. Close evaluation of the safety and tolerability of antiemetics is

Although these agents are equivalent in terms of efficacy, they vary in terms of side effect profiles and potential for drug-drug and drug-disease interactions. These factors, in addition to the patient's unique risk factor profile, must be considered when deciding which 5-HT₃ to use. For example, Goodin noted, dolasetron is associated with cardiovascular effects, and thus should be used with extreme caution in patients at risk for developing prolongation of cardiac conduction intervals. Granisetron and ondansetron have been shown to induce abnormal vision and dizziness in a minority of patients. Ondansetron (compared to dolasetron and granisetron) is associated with increased incidence of CNS side effects. The pharmacokinetic

bidities is necessary in patients receiving antiemetics and cardiotoxic chemotherapy.

Goodin addressed the issue of cardiotoxicity associated with 5-HT₃-receptor antagonists (RAs). She said that trials have *excluded* patients with congestive heart failure, cardiomyopathy, hypertension, and heart block as well as those using concomitant medications such as diuretics, antiarrhythmics, and antihypertensives. Caution must be used in susceptible patients. "Choose the 5-HT₃-RA with the least apparent cardiac effects," she recommended.

Goodin concluded that safe and effective therapy in older patients is a challenge and nurses need to individualize treatments, striving for the lowest risk of overlapping toxicities and the lowest risk of drug interactions.

For the patient to get the best treatment, collaboration between physicians, nurses, pharmacists, patients, and families is critical.

important to selection and use in the complex aging patient. For older patients who are often malnourished, uncontrolled CINV can result in loss of appetite, dehydration, electrolyte imbalance, and exacerbated malnutrition.

CINV can occur in an acute or in a delayed setting. Acute CINV occurs at the onset or during the initial 24 hours of treatment. Delayed CINV can occur up to 24 hours after chemotherapy. Anticipatory CINV is a conditioned response related primarily to previous poor control of acute or delayed emesis. Finally, breakthrough CINV refers to CINV that occurs despite preventative therapy.

Treatments for CINV include serotonin receptor antagonists such as ondansetron (Zofran®, GlaxoSmithKline, Research Triangle Park, NC), dolasetron (Anzemet®, Aventis Pharmaceuticals, Bridgewater, NJ), granisetron (Kytril®, Roche Laboratories, Inc., Nutley, NJ) and palonosetron (Aloxi®, MGI Pharma, Bloomington, MN). Neurokinin-1 antagonists, such as aprepitant, can be used. Other treatments include dopamine antagonists, corticosteroids, anti-anxiolytics, and antihistamines.

The effects of these drugs are enhanced when administered in conjunction with corticosteroids. "Indicated for CINV, the 5-HT₃-receptor antagonists are the *gold standard* for the prevention and prophylaxis of CINV associated with highly and moderately emetogenic chemotherapy," Goodin said.

parameters of ondansetron are affected in patients with hepatic impairment, requiring dose adjustments.

Goodin explained that these differences are accounted for by the fact that although the 5-HT₃-receptor antagonists share the same mechanism of action, they differ significantly in their metabolism by the cytochrome P450 system. Within this system, each 5-HT₃-receptor antagonist is metabolized by an assortment of enzymes, including CYP3A4, CYP2D6 and CYP1A2. These three enzymes account for almost all hepatic drug interactions. Therefore, consideration of the patient's medication profile is extremely important to reduce as much as possible any drug-drug interaction complications.

Comorbidities such as cardiovascular problems, which occur in 60% of patients; respiratory problems, which occur in 35% of patients; digestive and hepatobiliary problems, which occur in 32% of patients; and genitourinary problems, which occur in 26% of patients, play an important role in choosing treatment regimens for older patients. Other comorbidities include osteoarticular (21%), diabetes (11%), and neurologic/psychiatric syndromes (6%) (Gridelli et al., 2003). In fact, older patients have an average of three different diseases (Lindsey, Larson, Dodd, Brecht, & Packer, 1994). Goodin said that a careful evaluation of these comor-

An Older-Focused Nursing Approach to CINV Control

"When emetogenic chemotherapy is indicated, oncology nurses should strive not just for *control*, but for *prevention* of CINV," said Kathy Lynch, RN, BSN, OCN®. The outcome of unmanaged CINV can result in serious injury to older patients including serious metabolic disturbances, nutritional depletion and weight loss, aspiration, fractures related to falls, and deterioration of patients' physical and mental status.

The risk for developing CINV is as individualized as the physiologic changes

Drugs That Can Cause Acute Change in Mental Status

- Antiparkinsonian drugs
- Corticosteroids
- Urinary incontinence drugs
- Theophylline
- Emptying drugs
- Cardiovascular drugs
- H₂ blockers
- Antimicrobials
- Nonsteroidal anti-inflammatory drugs
- Geropsychiatric drugs
- Ear, nose, throat drugs
- Insomnia drugs
- Narcotics
- Muscle relaxants
- Seizure drugs

Note. Based on information from Lisi, 2000.

Nurses need to be aware that confusion is not a normal consequence of aging. Multiple etiologies may be responsible for mental changes, such as electrolyte imbalance, disease or metastases, chemotherapy or other medications, and multi-drug effects.

that occur in aging itself. Again, comorbidities, polypharmacy, and physiologic aging are factors to be considered. In addition, general nutrition status and weight and muscle loss are issues as well. In older patients, gastrointestinal absorption of dietary vitamin D, zinc, and calcium are decreased. Often diets lack protein and are higher in fat and carbohydrates. Older people tend to have lower albumin levels leading to increased risk of drug toxicities.

Older people also have high prevalence of depression, which can be compounded by the cancer diagnosis, unmanaged side effects, and fear of impending death (Gallo & Lebowitz, 1999).

"Confusion is not a normal consequence of aging," Lynch said. She emphasized that mental changes must be considered. Multiple etiologies may be responsible for mental changes, such as electrolyte imbalance, disease or metastases, chemotherapy or other medications, and multi-drug effects. Certain drugs can cause acute changes in mental status, such as anti-Parkinsonian drugs, corticosteroids, cardiovascular drugs, and seizure medications.

Lynch said that nurses should assess patients' support systems. "Is the patient able to monitor and manage therapy and side effects? What constitutes the patient's support system? Is there an available, accountable 'go to' person? What other resources can be marshaled? How will interim follow-up occur? Issues such as adherence and socioeconomic pressures factor into the patient's success in treatment," Lynch said.

Lynch provided a case study of a 69-year old male patient with a history of heavy cigarette smoking, current cigar smoking, moderate emphysema, hypertension, myocardial infarction, hypercholesterolemia, and social alcohol consumption who was taking multiple medications and had a family history of colon cancer. He was being treated with aggressive chemotherapy and radiation therapy, surgical excision, and post-operative chemotherapy. The case study

illustrated the need to assess the full spectrum of symptoms, polypharmacy, and best combinations of antiemetics during chemotherapy.

Oncology nurses must have a strong working knowledge of specific comorbidities, medication profiles, and conditions that may affect the safety of CINV management. Additionally, the oncology nurse must develop proficiency in distinguishing symptoms of toxicity related to medication interactions.

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Components of Nursing Assessment of Older Patients

- Physical health
 - General health
 - Performance status
 - Nutrition
 - Fluid balance
 - Cognitive status
- Socioeconomic
 - Is the caregiver in the home?
 - Costs and payment issues
- Polypharmacy
 - How many prescription drugs are being taken?
 - Which are necessary and which are unnecessary?
 - Are they appropriate for older patients?
 - Are there duplications?
 - What over-the-counter medicines and nutraceuticals (complementary and alternative medicines) are taken?

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