Polypharmacy, aging, and cancer. (Your Older Patient).

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ABSTRACT

The plethora of medications taken by older patients with cancer increases the risk for adverse drug reactions, drug-drug interactions, and nonadherence for this age group. Although polypharmacy can be an issue in any age group, it can especially be a problem for the elderly, who consume more medications than any other patient group. Factors such as the presence of multiple comorbid conditions, advances in pharmacotherapy, and increased availability of over-the-counter and herbal supplements for self-treatment can all contribute to polypharmacy in this population. Physiologic changes associated with aging may alter the pharmacokinetic and pharmacodynamics of drug metabolism, which, in turn, affects potential drug toxicities. The incorporation of preventive methods—such as patient and physician education, and regular medication list review and monitoring prior—to its occurrence is key to preventing polypharmacy. Clinical trials designed to better reflect the “typical” general elderly population as well as to consider the implications of cost, drug interactions/metabolism, and adherence are needed to substantiate our clinical practice when dealing with the largest subset of our cancer population.

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Polypharmacy, defined as concurrent use of several drugs, is not uncommon in the elderly and increases their risk of adverse drug reactions and interactions.[1] Besides adverse drug reactions and drug-drug interactions, other clinical sequelae of polypharmacy include nonadherence, increased risk of hospitalizations, and medication errors.

Although polypharmacy can be an issue in any age group, it can especially be a problem for the elderly, who consume more medications than any other patient group. It has been reported that the number of drugs prescribed for patients increases as they age. [2] This is likely due to the increased number of chronic diseases prevalent in this population. It has been estimated that 78% of patients older than 65 years are on medications, and that 39% regularly take five or more drugs. [3] Up to 90% of the patients in this age group are also reported to take over-the-counter drugs. [4] As “baby boomers” age and as new medications become available to prevent and treat medical conditions such as cancer, polypharmacy and its risks will grow.

Cancer and Aging

The connection between aging and cancer is significant, with more than 60% of all cancers occurring among those over age 65.[5] As the aging population increases and more people move into this high risk group—projected at 20% of our population (or 1 in 5 Americans) by the year 2030—there will be an increasing burden of cancer in the elderly and more demands will be placed on the medical and research establishment to respond to this burden. Older-aged Americans are an important target population for cancer research and cancer control.

The complexities of medical management in aging patients with cancer and comorbidities, availability of nonprescription medications, tendency to self-treat, and the prohibitive costs of some anticancer medications can all contribute to the increased potential for polypharmacy, and ultimately may affect treatment tolerance and outcomes. Despite concerns about polypharmacy, however, few data characterizing the extent of drug use in older patients with cancer exist. [6]

Factors Contributing to Polypharmacy

Older patients with cancer are especially vulnerable to various factors that may contribute to polypharmacy in this population. Medical advances have greatly increased the number of medications available to treat a variety of conditions. As older patients are more likely to have several chronic conditions, this can lead to care by more than one health-care provider, each of whom may prescribe a different medication to treat the same symptom.

Data have shown that 31% of individuals aged 65 and older use more than one pharmacy to fill prescription medications. This creates a situation where each pharmacy checks for potential problems only on those medications that its pharmacist knows the patient is (or is supposed to be) taking. [7]
As polypharmacy can increase the risk for adverse drug reactions, so can an adverse drug reaction lead to a dangerous cycle of polypharmacy when an adverse drug reaction is misinterpreted as a new medical condition requiring treatment. The original problem is only confounded or exacerbated by the additional medication, and the cycle is perpetuated. [8]

Many drugs that were once only obtainable by prescription, such as omeprazole and loratadine, are now readily available over-the-counter, and their use is on the rise. In addition, the purported health benefits and aggressive marketing of alternative therapies (e.g., herbal products, food supplements) as treatments for cancer have dramatically increased their use during the past decade. This increased availability of over-the-counter and alternative therapies has raised the tendency for older patients to self-treat their ailments.

Nahin et al recently performed an analysis in patients enrolled in the Ginkgo Evaluation of Memory (GEM) study and found many adults aged 75 and older used a wide variety of dietary supplements. [9] With an increased number of cancer clinical trials enrolling older participants, investigators should pay close attention to participant use of off-protocol dietary supplements and how such use might affect the drug or supplement under study.

Sequela of Polypharmacy

Drug Interactions

An exponential increase in the incidence of adverse drug reactions is observed with the addition of each drug to an existing regimen. [10] While taking two drugs increases the risk of an adverse effect by 6%, the use of eight or more medications raises the risk by almost 100%. [11] Other factors that may potentiate adverse drug reaction risk in the elderly include inappropriate prescribing of medications and changes in the pharmacokinetics and pharmacodynamics in the senior adult.

The risk of deleterious drug interactions increases with the addition of each anticancer medication to the drug regimen. Although articles on one-to-one drug interactions with chemotherapy have been published, data specific to the impact of poly-pharmacy on tolerance to cancer therapy are still scarce. [12] Wallace et al reviewed data from older patients receiving chemotherapy metabolized by cytochrome P-450. These authors noted that, on average, patients were taking six concomitant medications, including an average of two medications also metabolized by cytochrome P-450. [13] Additional medications used by older patients may include not only prescription medications but also self-treatment with nonprescription products. These interactions may result in both subtherapeutic or super-therapeutic drug levels.

Sokol et al found in their study that agents used to treat cardiovascular and gastrointestinal comorbidities were used by the highest percentage of patients. [6] Thus, a higher incidence of comorbid conditions in the geriatric population can have an impact on chemotherapy in patients with cancer. For example, older cancer patients with cardiac conditions may be receiving chemotherapeutic agents that affect heart function. Another example is the frequent use of laxatives in the older population and the concurrent administration of chemotherapy agents that have a laxative effect, which can cause dehydration and subsequent hospitalization in the older patient with cancer.

Medications that an older cancer patient receives for his or her comorbid conditions can also interact with chemotherapeutic agents. Cytochrome P-450 enzymes can be induced or inhibited by many commonly prescribed medications such as opioids, antidepressants, antibiotics, and antipsychotics. The metabolism of chemotherapeutic agents may be altered by the concurrent use of beta blockers and vasodilators, leading to altered hepatic blood flow and an increase in toxicity. [14,15]

Age-related decreases in glomerular filtration rate are well known. These physiologic declines coupled with comorbid conditions and the use of multiple drugs that further diminish renal function have the potential to pose serious clinical problems with the administration of some chemotherapeutic agents. Approximately 70% of a carboplatin dose is eliminated in the urine within 24 hours in patients with normal renal function. The concomitant administration of drugs that influence renal function (for example, a COX-2 inhibitor) in the older population, have a potential to exacerbate carboplatin toxicities.

Interactions With Herbal Products

Given that herbal products are usually complex mixtures of multiple active ingredients and that they are not subject to the same regulatory requirements as pharmaceuticals, the treatment with these “natural” products may unintentionally harm the older person. A substantial portion of the public perceives these products as safe, even though little is known about the biologic effects of these compounds. It is also likely that many adverse effects associated with herbal medicine and other dietary supplement use have not been recognized or reported, due to the fact that these products are not viewed as medications and their use is often not disclosed to the health professional.

A significant knowledge gap exists regarding alternative therapies in cancer patients and how these therapies may interact with more conventional treatment. For example, St. John’s wort (Hypericum perforatum) has been reported to induce cytochrome P-450 metabolism, thus affecting drug concentrations in some patients. [16,17] In addition, the metabolism of some chemotherapeutic agents, such as irinotecan, can be altered by St. John’s wort.

Nonadherence

While various factors can lead to nonadherence, the phenomenon correlates strongly with the number of medications given to a patient. Nonadherence is a key reason for many outpatient drug treatment failures, which can cause serious medical complications. Rates of nonadherence have been estimated at 25% to 59% among older patients. [18] The average rate of nonadherence in individuals with chronic diseases has been reported to be 50%. [18]

Age-related factors, such as the difficulty experienced by an elderly person in interpreting the importance of a medication
or the directions for its use may also lead to nonadherence. Gebhardt et al reported that 60% of older adults interviewed would discontinue a prescription drug without consulting a physician if they thought the medication appeared not to be working. [18] The knowledge base, cognition, hearing acuity, vision, memory, and physical condition of the older patient may all affect adherence, and these factors may be single or additive in nature.

The costs of multiple medications may prohibit the older patient on a fixed income from purchasing essential medications and can lead to nonadherence. An elderly patient being prescribed an oral chemotherapeutic agent with a high copayment may have to discontinue other medications in order to undergo the particular treatment. Medications that are not essential may take priority over essential medications because the cost-benefit ratio of each drug may not be fully explained to the older cancer patient. All these factors can not only affect treatment outcomes, but may perpetuate the cycle of polypharmacy as more drugs may be prescribed due to the perception of ineffectiveness of the existing treatment.

Financial Burden

In addition to the above consequences to polypharmacy, there may also be an increased financial burden on older patients and the overall healthcare system. Office visits for an adverse drug event increase from 9% of the population per year from age 25 to 44 years, to as high as 56.8% between age 65 and 74 years. [20] In 2000, it was estimated that medication-related problems caused 106,000 deaths annually at a cost of $85 billion. [21] Other estimated costs of medication-related problems include $76.6 billion in ambulatory care, $20 billion in hospitals, and $4 billion in nursing homes. [22]

Recommendations

The recognition of polypharmacy is the first step toward its prevention. An interdisciplinary team approach, including a clinical pharmacist, a geriatrician, and a clinical pharmacologist, is needed to optimize safe and effective cancer therapy. A comprehensive baseline assessment of the older patient helps in identifying situations where polypharmacy may occur. [23] Thus, an integral part of every clinic visit should include a review of the patient’s medication list (which should include supplements, over-the-counter products, and herbal products in addition to prescription medications); discontinuation of any nonessential medications; and evaluation of drug interactions, adverse effects, and patient adherence.

The "brown bag" approach—whereby patients bring in all their medications for their doctor to review—is also useful in identifying and preventing polypharmacy. [24] Instructions on medications can be reinforced. As patients will bring in both prescription and nonprescription medications, the amount of medications remaining in the bottles can be compared with the amount that should remain to help determine the extent of adherence. Multiple physician and pharmacy use can be determined by the labels on the bottles. This approach provides information about possible drug interactions, actual prescribed dosages of medications, and duplication of medications.

An expert panel comprised of thought leaders in geriatrics, clinical pharmacology, and psychopharmacology developed explicit consensus criteria for determining potentially inappropriate medications in the elderly. The updated Beers Criteria are applicable to the general elderly population and should be consulted when dealing with polypharmacy in older patients. [25] It is important to keep in mind the heterogeneity of the elderly (the concept of chronologic vs physiologic age) when prescribing medications. Medication choices must be patient- and context-driven, often representing a difficult balancing act between benefit and risk.

Polypharmacy can also be prevented by changing prescription habits. Prescribing medications without a found diagnosis intensifies the risk of polypharmacy. The benefit of adding a medication to a therapeutic regimen must be weighed against the possible problems that may result from the addition. It is also important to make the patient aware of the benefit-risk ratio for each additional medication.

Summary and Comments

Polypharmacy is a frequent and dangerous health-care problem for the elderly patient. With the number of older cancer patients continuing to increase, polypharmacy and the chronic use of multiple medications are a reality for this population. The consequences of polypharmacy involve adverse drug reactions, drug interactions, high medication costs, and nonadherence. Polypharmacy is sometimes overlooked because the symptoms it causes can be confused with symptoms associated with the normal aging process or another disease. Polypharmacy is often recognized after it has occurred. The incorporation of preventive methods prior to its occurrence is key to preventing polypharmacy.

Lastly, the majority of drugs prescribed to the elderly have previously been tested within randomized controlled trials on a biologically different and much younger cohort; thus, the optimal cancer treatment for this population is still unconfirmed. Research studies often do not consider the implications of cost, drug interactions, or nonadherence. Clinical trials designed to better reflect the "typical" general elderly population are sorely needed in order to substantiate our clinical practice when dealing with this largest subset of our cancer population. These studies should not only assess evidence of effectiveness but should also acknowledge the substantial burden of polypharmacy that characterizes the contemporary medical management of the older cancer population.

Reference Guide

Therapeutic Agents Mentioned in This Article

Carboplatin
Irinotecan
Loratadine
Omeprazole

Brand names are listed in parentheses only if a drug is not available generically and is marketed as no more than two trademarked or registered products. More familiar alternative generic designations may also be included parenthetically.

References


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