Review Article

Pharmacotherapy Considerations in Elderly Adults

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Abstract: Life expectancy for Americans has increased dramatically since 1900, as have the available pharmacotherapeutic options. Unfortunately, pharmacotherapy mishaps occur commonly in the older adult population. This problem greatly affects the morbidity and mortality of elderly patients and greatly increases healthcare costs. To improve patient care among elderly adults, healthcare practitioners must consider several issues when developing a pharmacotherapy plan. A thorough understanding of pharmacokinetics, pharmacodynamics, adverse drug reactions, drug interactions, and several other factors is necessary for practitioners to develop a safe and effective drug therapy plan for older adults. This review provides a general but comprehensive review of the issues pertaining to pharmacotherapy in elderly people and offers several suggestions for improving their pharmaceutical care.

Key Words: elderly adults, medication, pharmacology, pharmacokinetics

Elderly patients represent an extremely large and continuously growing population of healthcare consumers. The evidence-based guidelines developed for younger patients with specific disease states actually improve mortality such that the population of patients living to old age is increasing. Data from 2003 show that US life expectancy at birth for the total population was 77.5 years compared with 49.2 years at the turn of the 20th century.[2] As a group, elderly adults are difficult to distinguish. Patients can be classified as "young-elderly" (70–85 years old) or "old-elderly" (85 years old and older). This distinction may be important when evaluating drug studies in different age groups. Gender also can be used to distinguish patients. Because most elderly patients have more than one disease state and are prescribed many more medications than are nonelderly people, establishing definitive treatment guidelines can be difficult.[1–5]

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Treatment guidelines must be tailored to fit each elderly individual's specific pharmacology for prescribed drugs and for each patient's unique comorbidity or comorbidities. A specific pharmacotherapy regimen should be considered based on the patient's specific condition, disease states, and pharmacotherapy history. Establishing specific pharmacokinetic and pharmacodynamic profiles for specific drugs in individual patients is imperative to developing a well-tolerated and effective pharmacotherapy plan. This can be difficult to accomplish. Most new drugs are not studied in elderly patients and even less in elderly sick patients with various comorbidities who are taking a large number of different medications.[6–13]

The establishment of an individualized pharmacotherapeutic plan is possible only if careful consideration is undertaken regarding each drug's pharmacokinetic and pharmacodynamic profile in a specific patient. Because drugs may behave differently in different patients, a specific profile must be developed for each patient. Aspects of this profile can include the following:

- A drug's pharmacokinetic and pharmacodynamic profile in a specific patient
- The potential for drug interactions in a specific patient
- The potential for adverse drug reactions in a specific patient
- The issue of patient compliance with the pharmacotherapy plan

If each of these issues is considered, then a safe and effective pharmacotherapy plan can be established for each elderly patient.[7–12]

Pharmacokinetics

Pharmacokinetics describes how the body processes a specific drug after its administration. Every drug has a specific

Key Points

- Pharmacotherapy mishaps among elderly adults are a major healthcare issue.
- To develop a safe and effective pharmacotherapy plan, practitioners must consider the pharmacokinetics and pharmacodynamics of the drugs prescribed to older adult patients.
- Healthcare practitioners must consider several measures to reduce adverse drug reactions and drug interactions in elderly patients.
- Pharmacotherapy for elderly people can be improved by considering the pharmacology of medications and implementing an effective monitoring plan at the initiation of therapy.

pharmacokinetic profile based on specific parameters such as age, sex, weight, body mass index, hepatic function, and renal function. The more a specific drug is studied in specific patient types (eg, elderly patients), the better the understanding will be of the pharmacology of that drug in those patients. Proper doses can be established and a clear adverse effect profile can be determined.[1,14,15]

Drug researchers are hesitant to conduct large randomized controlled trials in elderly patients. Most elderly patients have several different diseases and take many different medications that cannot be discontinued so that a patient can participate in a drug study. The pharmacology of many medications in elderly adults has not been studied sufficiently, so making accurate predictions about pharmacokinetics in older adults is difficult. Developing an effective pharmacotherapeutic plan for an elderly patient requires a clear understanding of the principles of pharmacokinetics (absorption, distribution, metabolism, and elimination) and how the pharmacokinetics of a drug may be altered in the geriatric population, and this consideration must be applied to every drug that is prescribed.[1,14–18]

Absorption of Oral Medications

The gastrointestinal (GI) tract can change with age and this may affect how certain drugs are absorbed. The aging process can reduce GI motility and GI blood flow. Gastric acid secretion is reduced in older adults and this can result in an elevation in gastric pH. Increased gastric pH and reduced gastric blood flow may cause reduced drug absorption, whereas reduced GI motility may result in more of the drug(s) being absorbed. The age-related absorptive changes seen with fluctuating gastric pH also can be influenced by medication use. Concurrent use of antacids and overuse of proton pump inhibitors may contribute greatly to these changes.[19] Age-related absorptive changes can alter significantly a drug's absorption as well as its onset of action. The absorption of drugs that undergo first-pass metabolism also may be increased in older people. This action is seen with nitrates and the lipophilic β-adrenergic blockers (eg, propranolol).[14,17–19]

The net effect of these changes is difficult to predict and may vary depending on the nature of the drug being prescribed. Age-related changes affecting drug absorption are, by themselves, generally considered minimal, but elderly patients are at high risk for developing other problems that can affect absorption. These problems, which are common in older adults, include swallowing difficulties, poor nutrition, and dependence on feeding tubes.[14,17,18]

Distribution

Drug distribution refers to where the drug goes after it enters the bloodstream. For drugs that are administered orally, the distribution phase begins after absorption and first-pass metabolism. The distribution phase is represented by a theoretically calculated volume; however, no real volume exists. Rather, the apparent volume of distribution of a drug is illustrated by a proportion that relates the amount of drug in the body to the concentration of drug measured in a biological fluid. Some drugs are widely distributed into tissues, body fluids, and the central nervous system by crossing the blood-brain barrier. Other drugs are not distributed well at all, such that the apparent volume of distribution may be close to the actual volume of blood in the body.[1,14,15,17,18]

Various factors influence the volume of distribution of a drug, including protein binding (only unbound drug is distributed), pH, molecular size, and water or lipid solubility (lipid-soluble drugs, in general, have a greater volume of distribution). For instance, phenytoin is a highly protein (albumin)-bound anticonvulsant that may have a significant effect in elderly patients who have reduced albumin levels. This leaves more free phenytoin available to cause various adverse effects.

Understanding how and where a specific drug is distributed is vital information because this determines the dosage necessary to achieve an adequate concentration of the drug at the location where the drug has its primary effect (ie, specific body fluid or specific tissue or organ system). The distribution volume of a drug is determined via phase I trials mandated by the US Food and Drug Administration (FDA) before they approve a drug.[4,14,17,18]

The aging process can have a significant effect on how a drug is distributed in the body. As the body ages, muscle mass declines and the proportion of body fat increases; therefore, drugs that are fat soluble will, in general, have a greater volume of distribution in an older person compared with a young person, but for drugs distributed in muscle tissue, the volume of distribution may be reduced. This effect is observed with diazepam, which is highly fat soluble, and this may necessitate dosing changes until the desired effect is observed.

The aging process also is associated with a theoretical reduction in total body water, which can affect the volume of distribution of water-soluble drugs. Older adults in general produce less albumin, which binds drugs in the bloodstream. Reduction in protein binding can result in an increase in free drug concentration. As the free drug concentration increases (compared with bound drug), more drug becomes available to reach receptors, thus increasing the pharmacologic effect in an elderly individual.[14,17,18]

All of these effects taken together can greatly influence how a drug is distributed, and this ultimately determines the dose that is necessary to produce a desired pharmacologic effect or unwanted adverse effects. If the distribution volume of a drug is reduced in an elderly patient, then the loading dose that is necessary to achieve a desired concentration is reduced and the half-life of the drug (the time it takes for the blood concentration to decline by 50%) may be altered. Failure to take these changes into consideration can result in drug toxicity. Changes in the half-life of a particular drug also will determine the specific dosing regimen for a patient. If

a drug's distribution volume is increased, then the opposite effects occur.[14,17,18]

Consideration of how a drug's volume of distribution may be altered in an elderly patient is an important component that helps determine the proper drug dose for an individual. Drugs that have undergone sufficient study in elderly patients to determine how the volume of distribution will change because of aging can be dosed more precisely in this population. For drugs lacking such information, the dose should be reduced and titrated to a specific effect.[8–10,14,15,17,18]

Metabolism

The liver is the primary organ responsible for drug metabolism. The liver can both synthesize various proteins, substrates, and enzymes and convert chemicals (xenobiotics) from one form to another. This detoxification process is complicated, but the result is to convert substances believed to be harmful to the body to a form that can be eliminated more easily. In general, the final by-product of liver metabolism is a water-soluble product that is readily eliminated via the kidney; however, some toxins (eg, acetaminophen) can be converted to toxic components before being converted to the final by-product, which can pose problems if the final product cannot be synthesized.[14,15,18,19]

The liver uses various types of reactions to complete the transformation process. Oxidative reactions (phase 1) may occur via oxidation, reduction, hydrolysis, or other types of chemical conversions. Phase 1 reactions typically involve cytochrome P450 monooxygenase (CYP450) enzymes. There are various types of CYP450 enzymes and they can play a role in drug metabolism. The CYP450 system is also where many drug– drug interactions occur, because various drugs can act as inducers or inhibitors of other drugs undergoing metabolism. Some drugs must be converted via the liver to the active form of the drug (prodrugs). Phase 2 reactions are conjugative. Products of conjugation reactions have increased molecular weight and are usually inactive, unlike phase 1 reactions, which often produce active metabolites. Some drugs undergo both phase 1 and 2 metabolism.[14,15,17,18]

Alteration of the normal metabolic process can significantly affect the pharmacokinetics of a drug. If the normal route of metabolism is slowed in any way, then the half-life of the drug may be prolonged such that the potential for adverse drug reactions (ADRs) increases significantly. If the process is sped up in some way, then the half-life of the drug is reduced and the effectiveness of the drug may be altered. Metabolic capacity can be affected by many variables, including diet, genetics, alcohol, nutritional status, sex, and the presence (or absence) of interacting drugs.[1,4,5,17,18]

The aging process also can affect drug metabolism. Several physiological changes can greatly influence metabolic capacity. In general, hepatic blood flow is reduced in elderly adults, which can significantly affect metabolism because the drug is introduced to the liver at a much lower rate. Liver mass and intrinsic metabolic activity (includes the CYP450 enzyme system) also is reduced during the aging process. Phase 1 reactions are affected much more than are phase 2 reactions. With a reduction of blood flow to the liver and a reduction in metabolic activity, the metabolic process is significantly reduced in older adults.[15,17,18]

All of these effects are variable, which makes it difficult to measure the extent of hepatic function reduction and then quantitate this effect so that doses can be calculated based on liver function. Because age, sex, genetics, and other variables play such major roles in metabolic capacity, any formula for dose calculation based on hepatic function alone would not be accurate. Although no precise formula can be established based on liver function, the doses of hepatically cleared drugs in elderly patients should be reduced. Dosage adjustments are somewhat arbitrary, but in older adult patients, a general recommendation is to reduce the dosage for those drugs undergoing hepatic metabolism. The dose can then be titrated to efficacy or adverse effects.[1,14,15,17,18]

Excretion

Elimination of drugs from the body occurs primarily via renal excretion. As with metabolism, the half-life of drugs is increased as renal function is reduced. As the body ages, renal function declines, sometimes by a significant degree. This decline is the result of several physiological changes, which include a reduction in blood flow to the kidneys, a decrease in kidney mass, and a reduction in the size and number of functioning nephrons. Unlike hepatic effects, these changes are consistent from one patient to another.[14,17,18]

Different from hepatic changes observed with aging, renal changes can be somewhat predictive, thus allowing drug dose adjustment based on renal function that is either measured or calculated. Calculations based on laboratory measurements (eg, serum creatinine) or other data can be used to estimate a patient's renal function. In fact, pharmaceutical manufacturers use these estimates to provide dosing guidelines to healthcare providers for drugs that are eliminated primarily via the kidneys.

The impact of renal elimination of medications cannot be overstated. Many drugs are completely or partially excreted by the kidneys. Other drugs are metabolized (sometimes to active metabolites) and these metabolites are then excreted renally. A reduction in glomerular filtration rate is a noted consequence of aging. Knowing which drugs are excreted renally and knowing how to adjust the doses of those drugs in patients with renal impairment is imperative to ensure safe and effective drug dosing in all patients.[1,14,15,17–19]

There are several formulas that have been developed and assessed for estimating a patient's renal function. Two such formulas are the Cockcroft-Gault formula and the modification of diet in renal disease (MDRD) formula.[14,17,18] Two of these formulas are reviewed and compared to 24-hour measured creatinine clearance in Table 1. The Cockcroft-Gault formula is the most

Table 1. Formulas available for estimating creatinine clearance[1,14,15,17,18]

Creatinine clearance estimate	Formula	Comments
Cockcroft-Gault formula	Estimated creatinine clearance (mL/min) = [140 − age (y) × weight (kg)]/(72 × SCr) Multiply by 0.85 if female	Widely used; Cockroft-Gault equation is used to make dosage adjustments, because this is how drug manufacturers establish their dosing recommendations. This is mandated by the FDA.
	Use ideal body weight: Men = 50 + (2.3 × number of inches over 5 ft) Women = 45.5 + (2.3 × number of inches over 5 ft)	The process of rounding the SCr concentration up by 1.0 mg/dL is not supported by medical evidence.
Abbreviated MDRD equation	Estimated glomerular filtration rate (mL/min/1.73 m^2) = 186 × serum creatinine (mg/dL) $^{-1.154}$ × age (y) $^{-0.203:}$ • × (0.742 if female) • × (1.210 if African American)	May be most effective in patients with diabetic kidney disease, patients with chronic kidney disease in middle age (average age 51 y), black patients with hypertensive chronic kidney disease, and patients with preexisting kidney disease. The MDRD equation is often used to stage patients' degree of kidney dysfunction.
Actual 24-h creatinine collection	Time-consuming and increases work for nursing	Pregnant women, patients with extremes of age and weight, patients with malnutrition, patients with skeletal muscle diseases, patients with paraplegia or quadriplegia, patients consuming a vegetarian diet and with rapidly changing kidney function

Circumstances under which these equations are not effective for estimating renal function: extreme body weight: body mass index <19 or >35 kg/m^2, significant muscle mass abnormality (amputations, loss of muscle mass, muscle disease, or paralysis), acute kidney failure, pregnancy, severe hepatopathy, generalized edema, or ascites.
FDA, Food and Drug Administration; MDRD = modification of diet in renal disease; SCr = serum creatinine.

commonly used calculation, although many practitioners prefer the MDRD formula, which may prove to be more accurate than other formulas even though it has not been used for as long as Cockroft-Gault. In elderly adults, a low serum creatinine is not always indicative of normal renal function. Because older adults have lower muscle mass than younger people, low serum creatinine may not be indicative of normal renal function but rather indicative of a reduction in muscle mass. The same issue is noted in individuals with amputations, malnutrition, or muscle wasting. For patients in whom serum creatinine may not be an accurate indicator of renal function, an actual 24-hour creatinine collection may be necessary.[14,15,17,18]

There is much debate about which formula should be used for estimating creatinine clearance. The Cockroft-Gault formula was developed when the laboratory methods used to measure serum creatinine were not as accurate as today's methods; therefore, comparing the MDRD formula to the Cockroft-Gault formula can be difficult. (Another formula [Chronic Kidney Disease Epidemiology Collaboration equation] also has been suggested and it may offer advantages over the other formulas, although it is unclear which estimate would be best to use in elderly adults). Pharmaceutical manufacturers have long used Cockroft-Gault when recommending dosage adjustments for renally excreted drugs. These recommendations appear on a drug's package insert, which is approved by the FDA. Drug manufacturers will not change their recommendations until required to do so by the FDA. The FDA must compare and contrast the information regarding these formulas to determine what would provide the most accurate estimation of a patient's creatinine clearance.[20,21]

In summary, the altered pharmacokinetics observed in most elderly patients significantly affect the particular pharmacokinetics of a drug. These changes are summarized in Table 2. Although drug absorption is probably least affected by aging, when all of these parameters are taken in concert, significant medication accumulation can occur and this leads to drug toxicity. It can be difficult to calculate the doses of drugs that are hepatically cleared, so arbitrarily reducing the dose and closely monitoring the patient would be appropriate. Doses are more easily calculated for drugs excreted renally based on current drug information. Renally excreted drugs must be monitored closely and their doses must be adjusted when appropriate.

Pharmacodynamics

Pharmacokinetics is essentially the science of how the body affects the drug and pharmacodynamics is the study of how a specific drug affects the body. All drugs have specific mechanisms of action and various adverse effects that are caused by pharmacological interactions in the body. The aging process may induce more or less sensitivity to particular medications. This is especially noteworthy for drugs that affect the cardiovascular and/or central nervous systems. This process may be caused by the effects that certain drugs have on receptor sites. As the body ages, the affinity that some medications have at particular receptor sites may change. The

Table 2. Summary of pharmacokinetic changes observed with aging[5,7,9,14,15,17,18]

Pharmacokinetic parameter	Altered physiology with aging	Comments
Absorption	↓ Gastric secretion	Many drugs may diminish in their absorptive ability
	↑ Gastric pH	Time of onset of action may be delayed
	↓ GI motility	Absorption is the pharmacokinetic parameter least affected by aging
	↓ GI blood flow	
Distribution	↓ Total body water	Increased Vd of lipid-soluble drugs
	↓ Lean body weight	Increased free fraction of drug
	↓ Albumin	
	↑ Body fat	
Metabolism	↓ Enzyme induction	Reduced hepatic clearance of drugs
	↓ Hepatic mass	Increased potential for drug interactions
	↓ Hepatic blood flow	For elderly patients, dosage should be reduced for hepatically cleared drugs
	↓ Activity in mixed function oxydase system	
Elimination	↓ GFR	For elderly patients, drug accumulation will occur for renally cleared drugs
	↓ Renal blood flow	

GFR, glomerular filtration rate; GI, gastrointestinal; Vd, volume of distribution.

number of receptor sites also may change over time, which can affect the efficacy of some drugs.[1,5,15,18]

Because of the physiological aspects of aging, elderly adults also may be at high risk for certain drug adverse effects. For instance, anticholinergic/antihistamines frequently cause urinary retention. This may not be a problem for younger patients, but it may be a severe problem for older male patients with benign prostatic hypertrophy. Patients maintained on certain blood pressure medications for many years may experience sudden precipitous drops in blood pressure caused by age-induced orthostatic hypotension. These are basic adverse effects of drugs, but they are caused by age-related physiological changes.[22]

Many older patients are prone to the effects that certain drugs have on the central nervous system, including dizziness, sedation, seizures, and confusion. These effects pose problems for elderly patients, who can be extremely sensitive to any drug-induced action on the central nervous system. Other drug-induced pharmacodynamic effects manifested by aging include drug-induced renal toxicity, which can be a major issue, especially in elderly patients who are already experiencing renal problems.

The effectiveness of certain drugs that act on specific receptors may be diminished in elderly patients. β-Adrenergic blockers are known to have a diminished effect in older people, probably because of a loss of sensitivity in the receptor. Proper titration of doses and patient monitoring will ensure that the correct therapy is prescribed.[18]

Predicting the extent of drug-related pharmacodynamic changes can be difficult. Because older adults can be sensitive to the pharmacological actions of drugs, care should be used whenever new medications are initiated in them. Starting with lower drug doses and titrating the dose as tolerated may help to prevent unwanted drug-related pharmacodynamic effects (Table 3). An understanding about how to properly monitor patients for a specific therapeutic response and understanding various drug-related adverse effects also may help healthcare practitioners to ensure the desired pharmacodynamic effect. As an example, consider the antihypertensive prazosin. This peripheral α-adrenergic receptor blocker effectively reduces

Table 3. Drug classes that have potential pharmacodynamic changes in elderly adults[1–8]

Drug class	Potential pharmacodynamic issues	Comments
Antihypertensives	Orthostatic hypotension	Additive effect at lowering blood pressure
		Use with caution
		Start with lower dose
Benzodiazepines	Increased sensitivity (eg, drowsiness, confusion)	Use with caution
		Avoid other central nervous system–active drugs
		Use lowest tolerable dose
β -Adrenergic blockers (eg, propranolol)	β-receptors less responsive	May require greater β-blocker doses to have same effect
Anticoagulants (eg, warfarin)	Greater sensitivity to drug action	Initiate with lower dose
		Follow international normalized ratio closely
Diuretics	Greater sensitivity to drug action	Monitor blood pressure and electrolytes

blood pressure in most patients. A common adverse effect of prazosin in many elderly patients is first-dose syncope. Because the aging process can affect the ability of the body to recover from orthostatic changes, α-blockers are commonly associated with orthostatic hypotension and patients must be instructed to anticipate this adverse effect until they become familiar with how the drug works in their body.

ADRs/Drug Interactions

The risk for developing an ADR is estimated to be 20%.[23] It has been estimated that the risk for developing an ADR that requires hospitalization is approximately 10.7% for elderly patients as compared with 5.3% for the general population. The majority of ADRs requiring hospitalization are thought to be preventable. ADRs are considered the sixth leading cause of death in the United States.[23] The risk for developing an ADR is much higher in elderly adults than in the general population and this increased risk translates into greater mortality for elderly patients.[23,24] The total annual direct medical cost of medication-related problems in the United States is estimated to be $104.2 billion. Much of this owes to the development of adverse drug reactions in elderly patients.[22–24,27,28]

Some ADRs can be prevented, but practitioners must be judicious in the care, use, and monitoring of the medications they prescribe to their elderly patients. Pharmaceutical research brings new drugs to market every year. This science has been instrumental in allowing people to live longer. For elderly adults, however, these new drugs are a double-edged sword; on the one hand, they may improve mortality, but on the other hand, they can induce an unwanted reaction. One national survey showed that 50% of community-dwelling people older than 65 years use five or more prescription and over-the-counter medications per week, and 12% use ≥10. The sheer number of medications used by elderly patients contributes much to the development of ADRs. Table 4 lists drugs and their adverse effects that are commonly used by elderly adults.[22–24,28]

Table 4. Drugs that commonly cause problems in elderly adults[5,7,15,20,25,26]

Drug	Adverse effect
Nonsteroidal anti-inflammatory drugs (eg, ibuprofen, naproxen)	Gastrointestinal bleeding, renal dysfunction
Diuretics (eg, hydrochlorothiazide, furosemide)	Hypotension, dehydration, electrolyte disturbance
Warfarin	Bleeding, many drug interactions
Angiotensin-converting enzyme inhibitors (eg, lisinopril)	Hypotension, renal dysfunction
Antidepressants (eg, amitriptyline)	Confusion, hypotension, constipation
Opiates (eg, morphine)	Confusion, disorientation, constipation
Prednisone	Osteoporosis, gastrointestinal problems, hyperglycemia
Benzodiazepines (eg, lorazepam)	Drowsiness, confusion

ADRs that affect functional status are frequently observed in elderly patients. The following reactions are common:

- Anticholinergic symptoms
- Mental status changes
- Orthostatic hypotension
- Mood and behavior changes
- GI tract disturbances (constipation or diarrhea)

What is notable about this list is the commonality of many of these effects and that many drug classes can be involved in causing these adverse reactions. Because older adults, in general, take a number of medications, identifying the exact cause of a specific reaction can be difficult. Table 5 is an attempt to illustrate this issue further. Extremely common adverse drug effects are listed, along with common manifestations of the effects. Because these problems occur with drugs that are commonly taken by elderly people and they occur with many types of drugs and drug classes, identifying the exact problem and cause can be a difficult process. A patient may have been taking many of the possible culprits for some time, making identification even more difficult.[23,24]

A common cause of adverse drug reactions in elderly patients is drug interactions. This is not surprising considering that the number of medications taken by many elderly patients is high. Various studies have documented a direct correlation between number of medications and the risk of an adverse drug reaction. A study from Brazil reported that the potential drug interaction risk when patients are taking 2 to 3, 4 to 5, and 6 to 7 medications are 39%, 88.8%, and 100%, respectively.[29] Contributing to this problem are pharmacokinetic and pharmacodynamic changes. Essentially, elderly patients are "set up" to have numerous drug interactions, all of which may induce an adverse drug effect.[23,30–32]

Some medications induce problems because they can aggravate a specific disease state while treating another problem. Because most elderly patients have various comorbidities, this is a common problem in these patients (Table 6).[31,32]

Preventing medication problems in elderly people is difficult. Many patients take a large number of drugs over many years. Many physicians are reluctant to stop medications started by a different physician, so the drugs are continued and the list increases. The most important concept for all practitioners to remember is that ADRs in elderly adults are extremely common and the only way to prevent them is to look for them and learn how to properly monitor their occurrence.[29,31–35]

Polypharmacy

Polypharmacy may be defined as the number of medications (eg, using a large number of different medications prescribed by different providers), the necessity of the medications that are prescribed, or the complexity of a patient's problems. Whatever the definition, polypharmacy is an important issue in elderly patients. Sometimes this issue cannot be helped, but many times polypharmacy occurs simply because healthcare providers fail to communicate proper patient recommendations

Table 5. Common ADRs in elderly adults associated with various symptomatology and drug classes[21,25,26]

Adverse effect	Manifestation of effect	Possible drugs or drug classes involved	Comments
Anticholinergic effects	Dry mouth, blurred near vision, hypotension, exacerbated narrow-angle glaucoma, excessive sedation, confusion or disorientation, constipation, dizziness, impaired gait and balance, impaired sweating, urinary hesitancy, urinary retention	First-generation antihistamines (diphenhydramine), antipsychotics, antidepressants, gastrointestinal tract motility agents, certain analgesics (tramadol), over-the-counter cough and cold preparations, etc	Common adverse effects from commonly used drugs
			Adverse effects are many times additive (eg, constipation from anticholinergics + narcotics)
			Central nervous system adverse effects can be insidious and develop over several years
Mental status changes	Confusion (acute or chronic), excessive sedation (drowsiness to soporific states), delirium, trouble concentrating, cognitive impairment, memory loss, dementia, impaired gait and balance, deficits in judgment or orientation to time, place, or person	All drug classes listed above plus muscle relaxants; drugs that may affect electrolytes (diuretics); central nervous system effects from other drug classes (eg, digoxin, amiodarone)	Adverse effects are additive and insidious, difficult to distinguish from metabolic problems, practitioner must take careful drug history to discern
Orthostatic hypotension	Sudden drop in blood pressure, dizziness, falling down	All blood pressure medicines (eg, β-blockers, calcium channel blockers), narcotics, phenothiazines, antidepressants, others	Fall risk is a major problem
			If this effect results in a fall causing broken hip or other bones, it can be devastating for patient
			Many effects are additive
Gastrointestinal tract disturbance; urinary incontinence	Constipation, diarrhea, nausea, vomiting, bladder problems	Diuretics, anticholinergics, antibiotics, almost all drugs can cause some form of GI problem	Results in less interaction for patient
			Can cause noncompliance
			Can cause nutritional disturbances
			Can contribute to bed sores, etc
Cardiac changes	Prolonged QTc leading to heart rhythm abnormality	Anticholinergics, antipsychotics, atypical antipsychotics, erythromycin	Effect can be fatal
			May be more common in patients with electrolyte abnormalities or previous cardiac history

to the patient's primary care provider. If each patient had a primary healthcare advocate who coordinated the patient's overall care, then the risk of polypharmacy could be reduced. Effective communication between all of a patient's healthcare providers is key to eliminating this problem. One simple recommendation is to ask every patient to bring all of his or her current medications to each doctor's visit so that the physician can thoroughly review the medications being taken.[1,2,5,6]

Compliance

Compliance with the care that is recommended to a patient can be a constant battle and a complex issue of understanding, communication, language barriers, social and cultural issues, monetary problems, and so forth. These issues can be addressed, but only if patients and practitioners can communicate. Finding a way for all of the parties involved to communicate with one another is the key to reducing patient noncompliance.[1,2,4]

Poor compliance in elderly adults also may be a product of health literacy. Studies have shown that as health literacy declines in older people, mortality increases. Several issues

Table 6. Selected disease states that may be aggravated by medications[9]

Disease state	Aggravating drug	Potential adverse effect
Diabetes	Corticosteroids (eg, prednisone)	Drug-induced hyperglycemia
Osteoporosis	Corticosteroids (eg, prednisone)	Increased fracture risk
Constipation	Anticholinergics/ antihistamines/narcotics	All slow gastrointestinal tract motility
Parkinson	Antipsychotics	Aggravate movement disorder
Hypertension	Nonsteroidal anti-inflammatory drugs	Fluid retention increases blood pressure
Benign prostatic hypertrophy	Anticholinergics/ antihistamines	Urinary problems

related to health literacy affect older adults, including poor education, language barriers, and mental health issues (eg, dementia, agitation), and all of them must be considered to improve compliance.[1,35,36]

Tools for Appropriate Medication Decisions

Practitioners can use a number of tools to make appropriate medication decisions for their elderly patients. The Beers criteria is a list of medications that, based on the drugs' pharmacology (eg, mechanism of action, pharmacokinetics, adverse effect profile), may cause adverse effects in older people. The list was initiated in 1991 and an update was completed by the American Geriatrics Society in 2012. The criteria are intended to provide physicians and healthcare providers who treat elderly patients with a comprehensive list of medications that may be harmful to older adult patients. The updated criteria are composed of three detailed lists. The first list is classified as drugs that have been demonstrated to be problematic in elderly adults. The second classification lists drugs that may be inappropriate for older people who have certain diseases or risk factors. The third classification lists drugs that should be used with caution in elderly patients. Most of the medications on the lists are well known, and medical evidence supports their potential to be harmful in this patient class. The Beers criteria do not ban the use of drugs on the list for all elderly patients; instead, they emphasize the drugs that may pose the most harm so that they are used judiciously and with caution.[32,33]

Similar to but much more comprehensive than the Beers criteria is the Screening Tool of Older Persons' Prescriptions. Rather than a simple checklist of medications, it attempts to

Table 7. Methods to improve drug-related problems in elderly adults[1–7]

Medication issues	Comments
Improve compliance	Use as few drugs as possible
	Written instructions
	Council patient and family/caregiver
	Improve communication skills (eg, language)
	Make medications affordable
	Memory techniques (eg, calendars)
	Recognize potential health literacy issues that may cause compliance issues (eg, language issues, dementia)
Reduce polypharmacy	Use only 1 primary care provider who communicates with specialists
	Use only 1 pharmacy
	Reduce the number of drugs necessary because of adverse effects of another agent (eg, laxatives for drugs that cause constipation)
	Review all medications on each visit to doctor (brown bag)
	Maximize doses when possible instead of adding a new drug
Always consider pharmacokinetics/pharmacodynamics	Assess patient's renal function using specific formula on each visit (or obtain measured creatinine clearance)
	Establish any new or previous hepatic problems
	Ensure that patient can swallow and take oral medications
	Check for any weight loss or nutritional issues that can affect pharmacokinetics
	Assess for drug-induced changes in renal or hepatic function on each visit
Interactions	Assess for drug–drug interactions
	Assess for drug–disease interactions
Monitoring	Implement monitoring plan for every drug the patient is receiving and put this plan in writing
	Monitoring plan must include ways to monitor for beneficial effect as well as adverse effects
	Always make patient and/or caregiver part of the monitoring process
	Ensure that this plan is shared with all of the patient's healthcare providers, including other physicians, nurses, pharmacists, nursing facility, hospice
	Always make sure patient and/or caregiver understands why medications are being used and instructions for use
Communication	Patients must be able to communicate with their healthcare providers easily and must be encouraged to do so
	Healthcare providers must work together and must be able to communicate with one another to ensure that the best possible care is provided to the patient
	Physicians must be able to use the latest technology so that medical information is readily available for them to make proper pharmacotherapy plans
	Recognize potential health literacy issues that may cause communication problems

assess the use of a drug with a specific patient who has specific comorbidities.[32–35]

Whichever tool is used, the primary purpose is to prescribe medications to all elderly patients with care and consideration, which ensures that each older adult patient is provided with the best care possible. Achieving this goal will result in happy and healthy patients, less polypharmacy, fewer adverse drug effects, and lower healthcare costs.

Conclusions

Pharmacotherapy mishaps among elderly patients are a major healthcare issue and a problem for all healthcare practitioners treating elderly patients. Physicians, nurses, pharmacists, nurse practitioners, physicians' assistants, and patients' families and caregivers are responsible for improving the care provided to elderly patients. Effective communication is vitally important.

Table 7 is a list of specific methods that practitioners can use to improve pharmacotherapy for their elderly patients. Working with patients so that they can be compliant with their pharmacotherapy plan is extremely important. Practitioners' understanding the pharmacology of the drugs prescribed to elderly patients will help ensure that doses are appropriate. Implementing a thorough and thoughtful monitoring plan for the prescribed pharmacotherapy will help ensure that the medications are effective and help to catch any unwanted effects that may arise.

The type of pharmacotherapy that is available to physicians for fighting disease is extensive. The number of available drugs will continue to increase. These drugs are effective only if used prudently. Thoughtful consideration about every pharmacotherapy plan will help ensure that all patients receive the best care possible.

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