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Polypharmacy in the Elderly

Facts and Figures

Older people are likely to be taking more medications

Older people suffer from more illness, including chronic conditions. As the amount of illness increases, the amount of prescription medication use often increases as well. As this happens, it becomes ever more challenging to achieve an ideal balance between the risks and benefits of medications. This can lead to an increased risk of adverse drug events. It has been reported that the probability of an adverse drug event is 13% in patients taking 2 drugs, and increases to 82% in those taking more than seven (Goldberg et al, 1996). In patients taking 10 medications or more, this probability nears 100% (Nolan and O'Malley, 1988).

There is evidence of a trend of increasing medication use in the elderly. One study found that in 1998, 54% of elderly patients used more than 5 medications and 19% used more than 10. In 2003, these numbers were 67% and 28% (Jyrkka et al, 2006)

Adverse drug events commonly cause illness in the elderly

Among other things, adverse drug events (ADEs) include falls, cognitive dysfunction, bowel and bladder problems, gastro-intestinal problems, bleeding, postural hypotension, cardiac abnormalities, and electrolytic disorders. Estimates suggest that ADEs account for as many as 10-17% of hospital admissions in the elderly (ASCP Update, 2000; Hayes et al, 2007). Most are predictable and many are preventable.

ADEs rank 5th among the greatest and most preventable health threats to the elderly, after CHF, breast cancer, HTN, and pneumonia (Zagaria, 2000)

While taking more medications increases the risk of an adverse drug event, it is not the only, nor the most important, consideration. ADEs may arise from inappropriate prescribing causing the misuse, overuse, or underuse of medications. They may also arise when drugs interact with disease states, with other drugs, or with other consumed substances. Elderly people are especially vulnerable because aging affects how their body handles medications. It is important to weigh in many factors when prescribing medicine to the elderly.

RGPs OF ONTARIO

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CERAH Centre for Education & Research on Aging & Health

Recognize common ADEs and risky situations

Adverse drug events are often misdiagnosed in older people. The effects of medications are often altered due to consequences of aging such as the increased presence of chronic disease. As well, different people age in different ways, and this wide physiological variation makes it difficult to predict the effects that any medication might have. Complicating this even further is that drug reactions often mimic the signs and symptoms of disease, "fooling" clinicians into thinking that they are caused by an existing medical condition or by the onset of a new medical problem. Conversely, there are times when a physical reaction to a medication, such as fatigue or weight loss, are dismissed as being a part of "normal" aging.

Most common types of preventable ADEs:

- electrolytic/renal (27%)
- gastrointestinal tract (21%)
- hemorrhagic (16%)
- metabolic/endocrine (14%)
- neuropsychiatric (9%)

Most common medication categories associated with preventable ADEs:

- cardiovascular medications (24.5%)
- diuretics (22.1%)
- non-opioid analgesics (15.4%)
- hypoglycemics (10.9%)
- anticoagulants (10.2%)

From Gurwitz et al (2003) in a study of community-dwelling seniors

Physical signs that should arouse suspicion of an adverse drug reaction include fatigue, constipation, diarrhea, incontinence, weight loss, weakness, tremors, falls, drowsiness, dizziness, confusion, depression, agitation, anxiety, and decreased sexual behaviour. In particular, if the problem develops shortly after a medication is started or increased, a high level of suspicion for an adverse drug effect should be maintained. In addition to being aware of the side effect profile of the drug in question, the onset of these signs should be considered in the context of the patient's medical comorbidities, risk factors for illness, and previous response to this or other interacting medications. Note also that changes in health status, such as the ongoing evolution of an existing chronic condition, can affect a patient's sensitivity to a drug they may have tolerated previously for a long time.

Common drug classes and adverse reactions

Drug	Adverse Reaction
• ACE inhibitors	- hyperkalemia
• anti-inflammatory agents	- gastric irritation, ulcers, hemorrhage, anemia, blood loss, sodium retention, renal failure, may decrease effectiveness of antihypertensive drugs
• anticholinergics	- dry mouth, reduced gut motility, constipation, urine retention, confusion, sedation, orthostatic hypotension, blurry vision, falls
• anticoagulants	- bleeding complications, hemorrhage
• antidepressants (tricyclics)	- anticholinergic effects, heart block, falls, confusion, urine retention
• antipsychotics	- sedation, tardive dyskinesia, dystonia, anticholinergic effects, hypotension, falls, confusion, extrapyramidal side effects and Parkinsonism
• beta blockers	- bradycardia, heart failure, mild sedation, confusion, orthostatic hypotension, falls
• digoxin	- arrhythmias, nausea, gastrointestinal disturbance, anorexia
• diuretics	- thiazide diuretics and loop diuretics can cause hypokalemia, while potassium-sparing diuretics may lead to hyperkalemia
• hypoglycemic agents	- hypoglycemia, falls, confusion, brain injury
• narcotics	- decreased gut motility, constipation, sedation, confusion
• sedative hypnotics	- excessive sedation, confusion, gait disturbances, falls, impaired psychomotor skills

Data from Kane et al (1999), and Liu and Jackson (2008).

Patient characteristics can hint at a high risk for ADEs

In studies of adverse drug events, a number of common characteristics emerge that help predict individuals who may be at highest risk of an ADE. It is helpful to recognize the characteristics of this high risk population and to be especially vigilant when prescribing medications in this group of patients. Frail elderly patients are particularly vulnerable to adverse drug events due to age associated physiological changes. Furthermore, the majority of evidence-based drug treatment guidelines may not apply well to elderly individuals with multiple comorbidities, as the evidence typically is not obtained from this population.

High Risk Patient Characteristics

- 85 years of age or older
- low body weight or body-mass index
- more than 6 active chronic medical diagnoses
- atypical presentation of illness, recent hospital discharge
- 5 or more medications, or more than 12 medication doses per day, multiple health providers prescribing drugs
- history of previous adverse drug event
- impairment in cognition, vision, hearing, or dexterity
- factors affecting adherence to medications (eg. cultural, economic, physical, psychological, insufficient education about their prescriptions and over-the-counter drugs)

Age-Related Physiological Changes:

Pharmacokinetic changes – changes in drug processing and movement:

- decreased total body water and lower volume of distribution, leading to potentially higher concentrations of water soluble drugs (eg. lithium, ethanol, and digoxin) in the blood
- increased total body fat and volume of distribution, causing delayed effect and potential accumulation of lipid-soluble drugs (eg. long-acting benzodiazepines)
- liver metabolism: decrease in liver mass and blood flow; reduction in first pass metabolism of drugs such as beta-blockers, nitrates, tricyclic anti-depressants, benzodiazepines, thioridazine, and theophylline
- decreased kidney clearance prolonging drug half-lives; decreased serum albumin causing increased unbound concentrations of drugs like phenytoin, theophylline, warfarin, and digoxin

Pharmacodynamic changes – changes in end-organ physiological responses to drugs:

- increased response to drugs that act on the CNS (eg. benzodiazepines and opiates) due to changes in the blood brain barrier; increased response to warfarin
- decreased response to beta-agonists and beta-blockers

Inappropriate prescribing can lead to adverse drug events

When considering medication safety, just counting the number of drugs is not a clinically meaningful exercise. However, when a patient is exposed to more drugs, there is an increased chance that one or more have been prescribed inappropriately, or that there will be a drug interaction. Every prescribed drug should be indicated, when considered on its own and also holistically within the context of the patient's entire drug regimen along with factors such as comorbidities, drug interactions, physiology, and the patient's quality of life.

Signs of Inappropriate Prescribing

- prescribing medications that have no clear indication, that are inappropriate for use in the elderly, or that could be substituted with a safer alternative
- using duplicate drugs within the same medication class, or using drugs known to interact with one another
- drug dosage is too high or too low, indicated drugs are not prescribed
- symptoms are not identified as an adverse drug reaction and are treated with another drug – leading to a "prescribing cascade"
- clinical improvement when drug is stopped

Some drugs are not recommended in certain situations or to be used at all in elderly patients. Most commonly referenced are the updated Beers list (Fick et al, 2003) and the Canadian guidelines (McLeod et al, 1997). The Canadian guidelines have also been adapted into a quickly administered screening tool called IPET – the Improved Prescribing in the Elderly Tool (Naugler et al, 2000). Together, these tools warn of medications posing significant risk in the elderly, requiring careful clinical consideration when used instead of safer alternatives.

Underprescribing, when an indicated drug is not prescribed even though there is no reason to avoid using it, can result in unmet medical needs. Interestingly, it has been found that the probability of underprescribing increases as more drugs are taken (Kuijpers et al, 2008)

Sometimes it is not possible to avoid prescribing many medications, but this is not necessarily a bad thing if "thoughtful polypharmacy" is practiced. A good rule of thumb to follow when prescribing a new medication is to "start low and go slow."

Some common drug-drug interactions

DRUGS WHOSE EFFECT IS INCREASED BY ANOTHER

Drug/Drug Class	Effect increased by:	Clinical effect
• warfarin	- amiodarone, cimetidine, SSRIs, statins, isoniazid, triazole antifungals, metronidazole, sulfa drugs, zafirlukast, NSAIDs, anti-platelet medications, aspirin, heparin, dipyridimole, macrolides (eg. erythromycin, clarithromycin)	- increased risk of bleeding
• statins	- protease inhibitors, itraconazole, niacin, macrolides (eg. erythromycin, clarithromycin), itraconazole, diltiazem, verapamil, fibric acids	- myopathy, rhabdomyolysis
• sedative-hypnotics (eg. benzodiazepines)	- macrolides (eg. erythromycin, clarithromycin), other psychotropic agents with CNS effects, ethanol	- excessive sedation
• antidiabetic sulfonylureas	- sulfaphenazole, chloramphenicol, phenylbutazone, warfarin	- hypoglycemia
• phenytoin	- phenylbutazone - chloramphenicol - isoniazid	- nystagmus - cerebellar ataxia - sedation
• azathioprine	- allopurinol	- bone marrow suppressant
• methotrexate	- sulfisoxazole	- bone marrow suppressant
• digoxin	- diuretics, quinidine, amiodarone, macrolides	- digitalis intoxication
• propranolol	- cimetidine	- bradycardia
• calcium channel blockers (eg. nifedipine, felodipine amlodipine)	- ethanol	- risk of orthostatic hypotension acutely, loss of antihypertensive benefits in the long term
• venlafaxine	- triptans	- excess serotonergic activity
• ACE inhibitors (eg. ramipril)	- potassium sparing diuretics (eg. amiloride, triamterene, spironolactone)	- hyperkalemia, cardiac arrythmias

Data from Bressler R, and Bahl JJ (2003); Hayes at al (2007); Jensen (2008).

Some common drug-drug interactions

DRUGS WHOSE EFFECT IS DECREASED BY ANOTHER

Drug/Drug Class	Effect decreased by:	Clinical effect
• ASA	- ibuprofen	- decreased CV benefits, exaggerated GI toxicity
• codeine	- CYP2D6 inhibitors (eg. fluoxetine, paroxetine, hydroxychloroquine, propafenone, terbinafine)	- prevent conversion of codeine to morphine, reducing or nullifying analgesic benefits
• warfarin	- carbamazepine, barbiturates, phenytoin, rifampin, ritonavir, glutethimide, disopyramide, cholestyramine	- decreased anti-coagulation
• anti-hypertensives (eg. furosemide)	- NSAIDs	- sodium retention caused by NSAIDs can counteract hypertensive and diuretic effects
• statins	- cholestyramine, colestipol	- decreased absorption of drug
• thyroid supplements	- iron supplements, calcium	- decreased absorption of drug
• prednisone	- barbiturates	- decreased corticosteroidal effects
• quinidine	- barbiturates, rifampin	- decreased antiarrhythmic effect
• tetracycline	- antacids-iron	- decreased drug bioavailability
• metformin	- risperidone	- decreased hypoglycemic effects
• pioglitazone	- olanzapine	- decreased hypoglycemic effects

Data from Bressler R, and Bahl JJ (2003); Hayes at al (2007); Jensen (2008).

Some interactions between drugs and over-the-counter or herbal remedies

Herb(s)/OTC Remedies	Drug(s)/Drug Classes	Adverse Events
• gingko biloba	- warfarin, aspirin - thiazide diuretic - acetaminophen and ergotamine/caffeine	- increased bleeding risk - hypertension - subdural hematoma
• danshen, dong quai coenzyme Q, vitamin E, garlic, papaya	- warfarin	- increased INR and bleeding risk
• St. John's wort	- protease inhibitors, cyclosporine, theophylline, warfarin - digoxin - selective serotonin reuptake inhibitors	- induction of CYP450 3A4 system with decreased levels of drug available - decreased drug absorption from gut - lethary, incontinence, mild serotonin syndrome
• saw palmetto	- no specific drug interactions	- headaches, GI distress
• green tea	- warfarin	- increased clearance of drug
• ginseng	- warfarin - alcohol - phenelzine, MAOI	- decreased INR, increased clearance - increased alcohol clearance - headache, tremor, mania
• yohimbine	- tricyclic antidepressants	- hypertension
• senna, cascara	- possible interference with intestinally absorbed drugs	- decreased drug availability
• antacids	- anticoagulants - antibiotics (eg. tetracycline)	- decreased rate of absorption - decreased absorption
• antihistamines	- barbiturates, sedatives, pain relievers	- increased sedative effects
• decongestants	- diuretics	- hypertension
• iron supplements	- antibiotics	- decreased absorption of antibiotic
• salt substitutes	- diuretics, blood pressure medications	- hyperkalemia

Data from Fugh-Berman (2000), Hayes et al (2007), and Ohio Department of Aging (2007).

Some interactions between drugs and food/beverages

Drug Class	Interaction with Food/Beverage
• calcium channel blockers (eg. felodipine, nifedipine, verapamil)	- grapefruit juice can increase medication levels and side effects (breathing difficulty, irregular heartbeat, chest pain, dizziness)
• diuretics (eg. triamterene, spironolactone, amiloride)	- potassium-rich foods (eg. bananas, oranges, green leafy vegetables) can cause lightheadedness, fatigue, weakness, bradycardia
• blood thinners (eg. warfarin)	- should be consistent with vitamin K intake (foods high in vitamin K include green leafy vegetables, liver, lentils, garbanzo beans, and soybeans) as it interferes with warfarin function - alcohol, mango juice, and cranberry juice can increase risk of bleeding
• statins (eg. atorvastatin, lovastatin, simvastatin)	- grapefruit juice can increase side effects such as muscle weakness, atrophy
• fluoroquinoline antibiotics (eg. cipro-, levo-, moxi-, and nor-floxacin), tetracycline	- dairy products, vitamin/mineral supplements containing iron, zinc, or magnesium, and antacids taken within 2-4 hours can reduce absorption of the antibiotic
• benzodiazepines (eg. diazepam, temazepam, triazolam, midazolam), clomipramine	- grapefruit juice can increase side effects such as slowed breathing, hypotension, hallucinations, and confusion
• bisphosphonates (eg. alendronate, etidronate, risedronate)	- milk and dairy products, antacids, calcium-rich foods, and vitamins taken with these medications can decrease their absorption
• proton pump inhibitors (eg. pantoprazole)	- decreases absorption of nutrients like calcium, vitamin D, and perhaps iron; more fractures in those taking high-dose or long-duration PPIs

Adapted from Grey Bruce Community Coalition for the Prevention of Falls in Older Adults (2007). *Understanding Potential Interactions with Prescription Drugs.*

The uninformed patient is at risk of adverse drug events

It has been shown that age is negatively correlated with health literacy. It has been estimated the 16% of adults aged 65-69 have a poor understanding of health information, and this figure leaps to 58% for those 85 and older (American Medical Association, 1999). Careful effort needs to be made to ensure patients are well informed about the drugs they are taking.

An inverse relationship has been found between patient adherence and the total number of prescribed drugs. Poor adherence to drug therapy is common and often results when prescribed drug regimens are too complex, but also when patients are poorly informed of a drug's benefits and side effects, and when a patient's own goals and lifestyle are not considered. Educating patients about their medications and being available for needed counseling removes many obstacles to medication adherence.

Reasons for poor medication adherence

- too many drugs or too many daily doses
- confusion about dosing schedule
- inadequate knowledge of drug's purpose
- poor memory or cognition
- poor hand dexterity – too difficult to open packages
- intentional non-adherence trying to avoid unwanted side effects
- increased sensitivity to drugs causing toxicity or adverse effects

Elderly patients often have many co-morbid conditions and see a number of specialists, all of whom prescribe medications. If it is not possible to adhere to a single prescriber, clear communication is necessary to ensure fidelity of the patient's drug treatment program as a whole. Similarly, patients sometimes purchase their medications at different suppliers. They should be encouraged to use a single pharmacy and a relationship should be developed with their pharmacist, who can assist with providing accurate medication records, assist in patient education, and help identify risky potential drug interactions.

Patients themselves are the first-line witnesses to adverse drug reactions and physiological changes that can affect medication safety, as the onset of symptoms is likely to occur in the patient's home rather than in the health clinic. Enhancing communication between the health team and the patient is a key component in promoting safe medication use.