

Polypharmacy in older adults

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Mrs. B, age 66, presents to the emergency department with altered mental status, impaired gait, and tremors. Her son says she has had these symptoms for 3 days. He adds that she has been experiencing more knee pain than usual, and began taking naproxen, 220 mg twice daily, approximately 1 week ago.

Mrs. B's medical history includes coronary artery disease (CAD), gastroesophageal reflux disease (GERD), hip fracture, osteoarthritis, and osteoporosis. She also has a history of insomnia and bipolar disorder.

Further, Mrs. B reports that 2 months ago, after watching a television program about mental health, she began taking ginkgo biloba, 60 mg/d by mouth for "memory," and kava kava, 100 mg by mouth 3 times a day for "anxiety." She did not tell her physician or pharmacist that she began using these supplements because she believes that "natural supplements wouldn't affect her prescription medications."

In addition to naproxen, ginkgo biloba, and kava kava, Mrs. B takes the following medications orally: atorvastatin, 80 mg/d; aspirin, 325 mg/d; omeprazole, 20 mg twice daily; lithium, 300 mg twice daily; trazodone, 50 mg nightly; diphenhydramine, 50 mg nightly; calcium, 500 mg/d; vitamin D, 400 IU/d; and a daily multivitamin.

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Disclosures

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Mrs. B's blood pressure is 132/74 mm Hg (at goal for her age) and her laboratory workup is unremarkable, except for the following results: serum creatinine level of 1.1 mg/dL, blood urea nitrogen/serum creatinine ratio of 40, and creatinine clearance rate of approximately 85 mL/min. An electrocardiogram shows normal sinus rhythm with a QTc of 489 ms. A lithium serum concentration level, drawn randomly, is 1.6 mEq/mL, suggesting lithium toxicity.

Although there is no consensus definition of polypharmacy, the most commonly referenced is concurrent use of ≥ 5 medications.¹ During the last 2 decades, the percentage of adults who report receiving polypharmacy has markedly increased, from 8.2% to 15%.² Geriatric patients, defined as those age >65 , typically receive ≥ 5 prescription

Practice Points

- Ask patients which prescription medications, over-the-counter (OTC) medications, and dietary supplements or other "natural" products they use. Ask them to bring their medications to their office visit.
- Educate patients and their caregivers that the term "natural" is not synonymous with safe, and that even OTC medications have risks.
- Encourage patients to provide their pharmacist with an updated list of all prescription medications, OTC medications, and dietary supplements or other "natural" products they use so any potential interactions may be appropriately identified and addressed.

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Table 1

OTC medications and potential medication interactions

OTC medication/class	Medication and/or disease state interactions
Nonsteroidal anti-inflammatory drugs	Lithium: increased serum lithium concentrations Warfarin: increased risk of bleeding Drug-disease state interactions: chronic kidney disease, GERD, HTN, heart failure
Antihistamines	Anticholinergic effects: cognitive dysfunction, disrupted sleep, confusion, hallucinations, delirium, decreased vision and motor reflexes (may increase the risk of falls)
Antacids	Histamine-2 receptor antagonists may require dose adjustments in patients with renal insufficiency
Antispasmodics	Anticholinergic effects: cognitive dysfunction, disrupted sleep, confusion, hallucinations, delirium, decreased vision and motor reflexes (may increase the risk of falls)
Pseudoephedrine	Can exacerbate insomnia and agitation, proarrhythmic, seizures, hallucinations Drug-disease state interaction: HTN, benign prostate hyperplasia
Dextromethorphan	Morphine derivative, can result in dizziness and sedation
Laxatives	Overuse of laxatives may cause electrolyte disturbances or result in dehydration. Both of these could be proarrhythmic and can contribute to lithium toxicity

GERD: gastroesophageal reflux disease; HTN: hypertension; OTC: over-the-counter

Source: References 16-22

medications.² Polypharmacy is associated with increased¹:

- mortality
- adverse drug reactions
- falls
- length of hospital stay
- readmission rates.

Older adults are particularly vulnerable to the negative outcomes associated with polypharmacy because both increasing age and number of medications received are positively correlated with the risk of adverse events.³ However, the use of multiple medications may be clinically appropriate and necessary in patients with multiple chronic conditions. Recent research suggests that in addition to prescription medications, over-the-counter (OTC) medications and dietary supplements also pose polypharmacy concerns for geriatric patients.³ Here we discuss the risks of OTC medications and dietary supplements for older patients who may be receiving polypharmacy, and highlight

specific agents and interactions to watch for in these individuals based on Mrs. B's case.

Factors that increase the risks of OTC medications

Although older adults account for only 15% of the present population, they purchase 40% of all OTC medications.⁴ These patients may inadvertently use OTC medications containing unnecessary or potentially harmful active ingredients because of unfamiliarity with the specific product, variability among products, or decreased health literacy. According to research presented at a 2010 Institute of Medicine Workshop on Safe Use Initiative and Health Literacy, many patients have a limited understanding of OTC medication indications and therapeutic duplication.⁵ For example, researchers found that almost 70% of patients thought they could take 2 products containing the same ingredient.⁵ Most patients were not able to determine the

Clinical Point

Patients age >65 typically receive ≥5 prescription medications



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Clinical Point

Federal regulations do not provide a standard way to verify the purity, quality, and safety of natural medicines or supplements

active ingredients or maximum daily dose of an OTC medication. Patients who were older, had lower literacy, or were African American were more likely to misunderstand medication labeling.⁵ Additional literature suggests that up to 20% of medical admissions can be attributed to adverse effects of OTC medications.⁶

Misconceptions regarding dietary supplements

The use of alternative and complementary medicine also is on the rise among geriatric patients.⁷⁻⁹ A recent study found that 70% of older adults in the United States consumed at least 1 dietary supplement in the past 30 days, with 29% consuming ≥ 4 natural products. Women consumed twice as many supplements as men.¹⁰

The perceived safety of natural medicines and dietary supplements is a common and potentially dangerous misconception.¹¹ Because patients typically assume dietary supplements are safe, they often do not report their use to their clinicians, especially if clinicians do not explicitly ask them about supplement use.¹² This is especially concerning because the FDA does not have the authority to review or regulate natural medicines or dietary supplements.^{13,14}

With no requirements or regulations regarding quality control of these products, the obvious question is: "How do patients know what they're ingesting?" The uncertainty regarding the true composition of dietary supplements is a cause for concern because federal regulations do not provide a standard way to verify the purity, quality, and safety. As a result, there is a dearth of information regarding drug-dietary supplement interactions and drug-dietary supplement-disease state interactions.^{8,15}

What to watch for

*Table 1*¹⁶⁻²² (page 41) outlines OTC medication classes and potential medication and/or disease state interactions. *Table 2*²³⁻⁴⁵ (page 43) outlines potential interactions between select dietary supplements, medications, and

disease states. Here we discuss several of these potential interactions based on the medications that Mrs. B was taking.

Nonsteroidal anti-inflammatory drugs (NSAIDs). All OTC NSAIDs, except aspirin and salicylates, increase the risk for lithium toxicity by decreasing glomerular filtration rate and promoting lithium reabsorption in the kidneys.¹⁶ Additionally, NSAIDs increase the risk of developing gastric ulcers and may initiate or exacerbate GERD by suppressing gastric prostaglandin synthesis. Gastric prostaglandins facilitate the formation of a protective lipid-layer in the gastrointestinal (GI) tract.^{18,46-48} For Mrs. B, the naproxen she was taking resulted in lithium toxicity.

Ginkgo biloba is a plant used most commonly for its reported effect on memory. However, many drug-dietary supplement interactions have been associated with ginkgo biloba that may pose a problem for geriatric patients who receive polypharmacy.⁴⁹ Mrs. B may have experienced decreased effectiveness of omeprazole and increased sedation or orthostatic hypotension with trazodone.

Kava kava is a natural sedative that can worsen cognition, increase the risk of falls, and potentially cause hepatotoxicity.⁵⁰ The sedative effects of kava kava are thought to be a direct result of gamma-aminobutyric acid (GABA) modulation via the blockage of voltage-gated sodium ion channels.⁵¹ In Mrs. B's case, when used in combination with diphenhydramine and trazodone, kava kava had the potential to further increase her risk of sedation and falls.

Gastroesophageal reflux disease medications. Older adults may be at an increased risk of GERD due to diseases that affect the esophagus and GI tract, such as diabetes, Parkinson's disease, and Alzheimer's disease. Medications may also contribute to gastric reflux by loosening the esophageal tone. Nitrates, benzodiazepines, anticholinergics, antidepressants, and lidocaine have been implicated in precipitating or exacerbating GERD.⁵²

Table 2

Dietary supplements and potential medication interactions

Dietary supplement and common uses

Medication interactions

Ginseng <ul style="list-style-type: none"> • memory • cognition 	MAOIs: headache, tremors, mania-like symptoms Warfarin: decreases serum warfarin concentration
St. John's wort <ul style="list-style-type: none"> • antidepressant • mood enhancer 	SSRIs: drowsiness, potentiates serotonin and increases risk for serotonin syndrome Triptans: potentiates serotonin and increases risk for serotonin syndrome TCAs: decreases TCA effects, potentiates serotonin and increases the risk for serotonin syndrome Methadone: decreases methadone concentrations, case reports of precipitated withdrawal Benzodiazepines: decreases benzodiazepine serum concentrations 25% to 50% Digoxin: decreases serum digoxin level Statins: decreases statin efficacy Warfarin: decreases serum warfarin concentration Anticonvulsants: may decrease anticonvulsant effect Clozapine: decreases clozapine serum concentration
Kava kava <ul style="list-style-type: none"> • insomnia • anxiety 	Levodopa: potential dopamine antagonist effects CNS depressants: compound sedation and decreased motor reflexes; may put patients at an increased risk of falls
Black cohosh <ul style="list-style-type: none"> • estrogen replacement • hot flashes • rheumatoid arthritis 	Atorvastatin: may increase liver enzymes Cisplatin: may decrease cisplatin concentrations
Ginkgo biloba <ul style="list-style-type: none"> • cognition 	Anticonvulsants: may decrease the effectiveness of anticonvulsants Antipsychotics: may potentiate the effects of antipsychotics Warfarin: increases risk of bleeding
Ginger <ul style="list-style-type: none"> • acid reflux 	Warfarin: increases risk of spontaneous bleeding in patients taking >4 g/d
Garlic <ul style="list-style-type: none"> • cardiovascular support 	Aspirin: may increase bleeding time Clopidogrel: may potentiate effect of drug Warfarin: may potentiate the effect of the drug; doses >3 g/d are associated with an increased bleeding tendency; recommended to stop taking at least 1 week prior to surgery

MAOIs: monoamine oxidase inhibitors; SSRIs: selective serotonin reuptake inhibitors; TCAs: tricyclic antidepressants

Source: References 23-45

Clinical Point

Proton pump inhibitors should be prescribed sparingly and judiciously in geriatric patients

Numerous OTC products can be used to treat heartburn. Calcium carbonate supplements are typically recommended as first-line agents to treat occasional heartburn; histamine-2 receptor antagonists (H2RAs) and proton pump inhibitors (PPIs) generally are reserved for patients who experience heartburn more frequently.⁴⁷ Per the

American Geriatrics Society Beers Criteria for Potentially Inappropriate Medication Use in Older Adults, H2RAs were removed from the “avoid” list for patients with dementia or cognitive impairment due to a lack of strong evidence; however, H2RAs remain on the “avoid” list for patients with delirium.¹⁷ Low-dose H2RAs can be used

Clinical Point

Most patients cannot navigate the nuances of medication indications, maximum doses, and therapeutic duplications

safely in geriatric patients who have renal impairment. Although PPIs are not listed on the Beers Criteria, they have been associated with an increased risk of dementia, osteoporosis, and infections.^{53,54} There is robust evidence to support bone loss and fractures associated with chronic use of PPIs. However, the data linking PPI use and dementia is controversial due to multiple confounders identified in the studies, such as concomitant use of benzodiazepines.⁴⁸ PPIs should be prescribed sparingly and judiciously in geriatric patients, and the need for continued PPI therapy should frequently be reassessed.⁴⁸ Mrs. B's use of omeprazole, a PPI, may put her at an increased risk for hip fracture compounded by an elevated fall risk associated with other medications she was taking.

Trazodone causes sedative effects via anti-alpha 1 activity, which is thought to be responsible for orthostasis and may further increase the risk of falls.⁵¹ Mrs. B's use of trazodone may have increased her risk of sedation and falls.

Antihistaminergic medications are associated with sedation, confusion, cognitive dysfunction, falls, and delirium in geriatric patients. Medications that act on histamine receptors can be particularly detrimental in the geriatric population because of their decreased clearance, smaller volume of distribution, and decreased tolerance.^{17,18}

Anticholinergic medications. Although atropine and benztropine are widely recognized as anticholinergic agents, other medications, such as digoxin, paroxetine, and colchicine, also demonstrate anticholinergic activity that can cause problematic central and peripheral effects in geriatric patients.⁵⁵ Central anticholinergic inhibition can lead to reduced cognitive function and impairments in attention and short-term memory. The peripheral effects of anticholinergic medications are similar to those of antihistamines and may include, but are not limited to, dry eyes and mouth via increased inhibition of acetylcholine-mediated muscle contraction of salivary glands.⁵⁵ These effects can be

compounded by the use of OTC medications that exhibit anticholinergic activity.

Diphenhydramine causes sedation through its activity on cholinergic and histaminergic receptors. Patients may not be aware that many OTC cough-and-cold combination products (such as NyQuil, Theraflu, etc.) and OTC nighttime analgesic products (such as Tylenol PM, Aleve PM, Motrin PM, etc.) contain diphenhydramine. For a geriatric patient, such as Mrs. B, diphenhydramine may increase the risk of falls and worsen cognition.

Teach patients to disclose everything they take

Polypharmacy can be detrimental to older patients' health due to the increased risk of toxicity caused by therapeutic duplication, drug-drug interactions, and drug-disease interactions. Most patients are unable to navigate the nuances of medication indications, maximum dosages, and therapeutic duplications. Older adults frequently take OTC medications and have the greatest risk of developing adverse effects from these medications due to decreased renal and hepatic clearance, increased drug sensitivity, and decreased volume of distribution. Dietary supplements pose a unique risk because they are not FDA-regulated and their purity, quality, and content cannot be verified. Educating patients and family members about the importance of reporting all their prescription medications, OTC medications, and dietary supplements to their pharmacists and clinicians is critical in order to identify and mitigate the risks associated with polypharmacy in geriatric patients.

CASE CONTINUED

Mrs. B is diagnosed with lithium toxicity due to a drug-drug interaction with naproxen. Her lithium is held, and IV fluids are administered. Her symptoms resolve over the next few days. Mrs. B and her son are taught about the interaction between lithium and NSAIDs, and she is counseled to avoid all OTC NSAIDs

other than aspirin. Her clinician recommends taking acetaminophen because it will not interact with her medications and is the recommended OTC treatment for mild or moderate pain in geriatric patients.^{17,56}

Next, the clinician addresses Mrs. B's GERD. Although Mrs. B had been taking PPIs twice daily, her physician recommends decreasing the omeprazole frequency to once daily to minimize adverse effects and pill burden. She also decreases Mrs. B's aspirin from 325 to 81 mg/d because evidence suggests that when used to prevent CAD, lower-dose aspirin is effective as high-dose aspirin and has fewer adverse effects.⁵⁷ Finally, she advises Mrs. B to stop taking ginkgo biloba and kava kava and to always check with her primary care physician or pharmacist before beginning any new medication, dietary supplement, or vitamin.

Mrs. B agrees to first check with her clinicians before following advice from mass media. A follow-up appointment is scheduled for 2 weeks to assess renal function, a lithium serum concentration, and adherence to her simplified medication regimen.

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Related Resources

- US Department of Health and Human Services. National Institutes of Health. MedlinePlus. Herbs and supplements. https://medlineplus.gov/druginfo/herb_All.html.
- US Department of Health and Human Services. National Center for Complementary and Integrative Health. <https://nccih.nih.gov/>.

Drug Brand Names

Atorvastatin • Lipitor	Lithium • Eskalith, Lithobid
Atropine • Atropen	Methadone • Methadose
Benzotropine • Cogentin	Morphine • Kadian,
Clozapine • Clozaril	Morphabond
Clopidogrel • Plavix	Paroxetine • Paxil
Colchicine • Colcris,	Trazodone • Desyrel
Gloperba	Warfarin • Coumadin,
Digoxin • Cardoxin, Digitek	Jantoven
Lidocaine • Lidoderm,	
Xylocaine Viscous	

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Clinical Point

Tell patients to report all their prescription medications, OTC medications, and dietary supplements to their clinicians

Clinical Point

Acetaminophen is the recommended OTC treatment for mild or moderate pain in geriatric patients

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