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Polypharmacy: Optimizing medication use in elderly patients

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Abstract: The elderly are under-represented in drug trials, yet they are the greatest consumers of medications. A study examining randomized controlled trials of four commonly used medications found that the proportion of older patients (> 65 y) enrolled was significantly lower than the proportion in the average population; of 155 trials, only three dealt exclusively with the elderly. Despite the higher prevalence of many conditions (eg, hypertension, diabetes) in the elderly,...

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Full text: Mrs. Archibald, a 92-year-old woman, has been a customer at your pharmacy for many years. When her son, Ken, comes in to pick up her monthly blister packs, you tell him that she's been started on another medication and she now needs to use two blister packs daily to hold all of her 17 medications. Ken sighs heavily and says it's hard to get her to take the medications she already has. She's getting dizzy and confused, her nausea is worse, and she hardly eats. She's had several falls recently and is now afraid to go out. The elderly represent one of the fastest growing segments of the population and their use of medication is increasing significantly. In Ontario, from 1997 to 2006, the population older than 65 years of age increased by 18% while their claims to the provincial drug benefit program increased by 214%. The Canadian National Population Health Survey recently showed that 53% of seniors living in healthcare institutions, and 13% of those living in the community use five or more medications, with older seniors taking more medications than younger seniors. (2) This is consistent with Canadian Institute for Health Information data that show 23% of those older than 65 years of age and 30% of those older than 85 years of age had claims for 10 or more drug classes in 2009. Mrs Archibald's medication load is not that unusual.

The term polypharmacy refers to the use of multiple medications, typically five or more. (4) Recently, it has been used to describe the use of inappropriate medications, or more medications than clinically indicated. The prevalence of inappropriate medication use in the elderly ranges from 11.5%-62.5%. (5)

Consequences of polypharmacy include adverse drug reactions and interactions, nonadherence, increased risk of cognitive impairment, impaired balance and falls, and increased risk of morbidity, hospitalization, and mortality. (6-11)

In a recent Canadian study, almost half of the 27% of seniors regularly taking five or more medications experienced an adverse effect requiring medical attention. (4) Of 661 community-dwelling seniors surveyed, 25% reported an adverse effect, with one-third of these considered ameliorable and 11% preventable; an increased number of medications was associated with an increased risk of adverse reactions. (12) Adverse drug reactions account for a significant portion of emergency room visits and hospitalizations - many preventable if they had been identified earlier. (13-14) Ultimately, the more medications taken, or the more potentially inappropriate medications prescribed, the higher the likelihood of serious adverse effects requiring medical attention. (15-17)

Why are the elderly at risk for polypharmacy and adverse drug reactions?

As people age, they develop more chronic conditions, often resulting in more medications prescribed. Prescribers are often reluctant to change drugs other prescribers (specialists or hospitalists) have started, and may have difficulty recognizing medication side effects, thus increasing the risk of prescribing cascades (ie, new medications added to manage side effects). (1) Pharmacokinetics and pharmacodynamics also change as people age, and very few clinical studies have been conducted in the elderly.

AGE-RELATED CHANGES

With advancing age, progressive functional decline in organ systems (eg, kidney, liver) leads to changes in the way medications are handled and expressed.²⁰ Pharmacokinetic changes are outlined in Table 1.²¹⁻²² As little pharmacokinetic data are available for the elderly, we must make assumptions about what drugs might be affected.

Pharmacodynamic changes (ie, physiologic and biochemical effects of drugs on the body) with aging include increased sensitivity to cardiovascular medications, anticoagulants, opioid analgesics, antipsychotics, and benzodiazepines.²³ Altered concentrations of neurotransmitters and receptors, as well as altered receptor binding properties and responsiveness, are thought to contribute to pharmacodynamic changes resulting in exaggerated drug effects. Functional reserves decline with age, affecting the cardiovascular, musculoskeletal, and central nervous systems; this can also predispose the elderly to exaggerated drug effects. Impaired homeostatic mechanisms can result in more pronounced side effects (eg, orthostatic hypotension with antihypertensives) or lack of compensatory responses (eg, impaired reflex tachycardia, impaired regulation of temperature and electrolytes).^(20,23,24)

Patients previously stabilized on certain doses of medications may gradually begin to develop side effects over time because of these various changes. These side effects may be mistaken for new diseases, with new medications added for treatment.

LACK OF EVIDENCE FOR MEDICATION USE IN THE ELDERLY

The elderly are under-represented in drug trials, yet they are the greatest consumers of medications.²⁵ A study examining randomized controlled trials of four commonly used medications found that the proportion of older patients (> 65 y) enrolled was significantly lower than the proportion in the average population; of 155 trials, only three dealt exclusively with the elderly. Despite the higher prevalence of many conditions (eg, hypertension, diabetes) in the elderly, exclusion criteria limit their enrollment in trials. The "healthy elderly" subjects included in clinical trials do not represent the population that would typically use these medications. Therefore, despite the wealth of guidelines available for chronic disease states (eg, hypertension, diabetes, cardiovascular disease), few specifically address how to approach the very old or frail elderly.²⁶⁻³⁰ Adhering to guidelines often results in the addition of medications without considering remaining life expectancy, goals of care, and time to potential benefit of medications.³¹

Ken is clearly worried about his mom. You wonder whether her recent symptoms could be drug induced. You offer to take a closer look to see if any medications might be causing problems and whether her regimen can be simplified. You book an appointment to visit his mom at home and Ken happily pays the fee. He says having someone review all of her medications and work with the family doctor would be a great help.

Strategies for reducing polypharmacy

Pharmacists can take many practical and relatively easy steps to help reduce polypharmacy and promote medication adherence. Conducting a medication review for an older person taking many medications can be challenging but rewarding. Providing education and medication reduction suggestions to prescribers can reduce the overall number of medications and inappropriate medications.³³⁻³⁴ Stopping medications is an effective and safe approach to reducing polypharmacy. (3S) Interventions such as computerized decision-support systems and pharmacist involvement in multidisciplinary teams (eg, geriatric medicine services) can also positively affect prescribing.^(37,38)

STEP 1 DETERMINE "CAN THIS BE CAUSED BY A DRUG?"

One of the simplest ways to address polypharmacy is to use screening criteria to help identify potentially inappropriate medications (PIMs) in the elderly: medications with no clear evidence-based indications; medications that carry a substantially higher risk of adverse effects; or medications that are not cost-effective. Two commonly used screening tools are the Beers and STOPP criteria (Table 2^{q-m}) which differ slightly in content and sensitivity for detecting drug-related problems. They can be applied manually by visually comparing

a patient's medication list to each set of criteria or they can be incorporated into clinical decision support systems that flag PIMs at the time of prescribing. A strong association exists between medications listed in Beers and STOPP and poor patient outcomes (eg, adverse reactions, hospitalization, mortality).³⁹ Using these criteria does not replace the need for clinical judgment and understanding of a patient's values and needs; sometimes a PIM might be appropriate if the benefits outweigh the risks.

A quick check tells you that Mrs. Archibald is taking three medications that appear on both the Beers and STOPP lists: lorazepam, metoclopramide, and glyburide.

Considering whether a patient's abnormal signs or symptoms might be the result of a medication, whether it is a PIM or not, is a key step in determining which drugs might be causing problems. Linking potential side effects with causative drugs requires knowledge of the pharmacology of each drug, its known side effects, and the time of onset in relation to starting the drug. This approach is consistent with the "therapeutic thought process" developed by Winslade and Bajear.⁴ Keep in mind that some side effects can manifest gradually as pharmacokinetic and dynamic parameters change in an individual, or quickly if parameters change rapidly during acute illness. Medications that may contribute to common geriatric presentations are outlined in Table 3.^(10,42-50)

You think about Mrs. Archibald's recent symptoms- dizziness, falls, confusion, and nausea- and believe they might be related to her medications. Lorazepam could be causing dizziness, confusion, and falls. The many antihypertensive medications she is taking can all reduce blood pressure, which might result in dizziness, and hence falls. With a few questions, you determine that the nausea started soon after her metformin dose was increased. That's when the metoclopramide was started. Is this a prescribing cascade?

Prescribing cascades occur as a result of treating side effects of medications.⁵ For example, furosemide prescribed for a patient might cause urinary frequency. Oxybutynin is prescribed to manage the urinary frequency. Oxybutynin leads to confusion and behavioural disturbances and an antipsychotic is prescribed. As the list of medications grows, it becomes more difficult to sort out which medications were prescribed to treat medical syndromes as opposed to drug-related adverse effects. Ultimately, the cumulative effects of multiple medications can lead to more serious complications (eg, falls, delirium). Identifying and dealing with prescribing cascades requires a thorough history, including the timing of new symptom onset in relation to medication starts or changes. Table 4 lists some common prescribing cascades the authors have seen in practice.

STEP 2 DETERMINE WHICH DRUGS ARE STILL PROVIDING BENEFIT

Determining which medications are still providing benefit can be more challenging than identifying PIMs. This is an important step in the pharmacotherapy workup described by Cipolle et al.^(S2) A good initial approach is to ask about the symptoms (eg, pain, sleep) for which each symptom-based drug is being used. Next, look at signs (eg, blood pressure, blood glucose) to help determine whether medications used to treat hypertension and diabetes are needed. Keep in mind the need for more conservative blood pressure and diabetes targets in the frail elderly to reduce the risk of hypotension and hypoglycemia, respectively.⁵³⁵⁶

In discussion with Mrs. Archibald, you find out that metoclopramide has not helped her nausea. You also discover that she started taking glyburide regularly again at the same time as her metformin dose was increased. She had been taking glyburide sporadically previously. When the doctor said her diabetes was out of control, and the pharmacist started making blister packs for her, she decided to start taking everything again. Her blood sugar log shows several recent readings between 3 and 4 when she gets up in the morning. You check her blood pressure to find that it's 105/60. She's taking four antihypertensives.

Assessing the continued benefit of preventive medications is likely the hardest step. As noted earlier, few clinical trials included frail elderly individuals, so we know little about benefit versus risk in this population. For example, in situations of no other compelling indication (eg, angina, atrial fibrillation), the proven benefit of a beta-blocker post-myocardial infarction, in terms of reducing cardiovascular mortality, has been shown for only two years, yet guidelines recommend indefinite therapy.⁵⁷ Appropriate duration of treatment for acute

conditions is also often unclear. For example, four to eight weeks of proton pump inhibitor therapy is adequate for uncomplicated reflux or ulcers, yet many patients take them daily for years.

STEP 3 PRIORITIZE DRUGS FOR TAPERING AND STOPPING, DEVELOP A PLAN, COORDINATE AND COMMUNICATE WITH PRESCRIBER AND PATIENT

When deciding which medications to stop first, it is important to balance clinical impact (eg, reduction in side effects) with the risk of adverse drug withdrawal events (ADWEs, defined as clinically significant signs or symptoms caused by stopping a drug).⁵⁸ They can manifest as physiologic withdrawal reactions (eg, tachycardia with beta-blocker discontinuation), appearance of new symptoms (eg, sweating with antidepressant withdrawal), or exacerbation of an underlying condition (eg, worsening angina after stopping nitrates).⁵⁸ Table 558,⁵⁹ lists drugs that often have ADWEs. Factors that make ADWEs more likely are long duration of use (eg, benzodiazepines), higher dose (eg, corticosteroids), and short half-life (eg, paroxetine). Patient risk factors include a history of drug dependence or abuse and lack of buy-in. Certain medications are often tapered to reduce the incidence and severity of ADWEs. To successfully discontinue unnecessary or inappropriate medications, it is important to know which drugs can be stopped abruptly and those that should be tapered. It can be challenging to get patient and prescriber acceptance of the need to reduce medication dose, or discontinue or "deprescribe" unnecessary medications. Patient buy-in is important; in the absence of any acute adverse medication effects, collaboration with the patient can assist in deciding which medications to stop first.

Asking a few simple questions can facilitate this process:

- * What questions do you have about your medications?
- * Which medications do you feel most strongly about keeping?
- * Which medications do you wonder about with respect to how well they're working for you?

Talk about the goals of care with the patient, family, and physician. Typically, in the very elderly, goals are to maintain and improve physical function (eg, activities of daily living), psychological function (eg, cognition, depression), social function (eg, social activities, support systems), and overall health (eg, general health perception).

Mrs. Archibald repeats that the metoclopramide does not help her nausea. Her appetite is terrible and she does not want to go out with friends. She wants to keep acetaminophen- it effectively treats her knee pain and helps her get around the house. Her diabetes, diagnosed three years ago, is not a big bother; she doesn't think she needs all that medication. You start preparing a note to Mrs. Archibald's family physician. It's important to inform the physician that metoclopramide did not improve Mrs. Archibald's nausea. You suggest lowering the dose gradually and stopping metoclopramide over the next couple of weeks. Metoclopramide would be a good medication to prioritize tapering because of its potential to cause Parkinson-type symptoms (which you learned from the Beers and STOPP criteria). You include in your note that Mrs. Archibald's nausea started soon after the metformin dose was increased, which coincided with her starting to take all of her diabetes medications again; it is severely affecting her quality of life. You note her recent low blood sugars and suggest reducing metformin back to the previous dose and switching glyburide to an equivalent dose of once-daily gliclazide MR to reduce the risk of hypoglycemia. You note that you will ask Mrs. Archibald to continue monitor her nausea and blood glucose, and you will update the physician with changes.

When preparing patients for medication discontinuation, make sure to offer safer alternatives, including nonpharmacologic approaches (eg, distraction techniques for pain management, sleep hygiene approaches instead of sedatives). Prepare patients by discussing anticipated withdrawal effects and involve them in monitoring for ADWEs. Let the patient know that several attempts at withdrawal may be needed. Regular follow-up will also provide support and reassurance. Use a variety of communication tools including verbal and written, and use tapering calendars for more complicated cases.

After successfully stopping metoclopramide and eliminating the nausea and low blood sugar readings by reducing the metformin dose and changing from glyburide to gliclazide, Mrs. Archibald calls to thank you. She is

still dizzy, tired, and confused during the day and wonders if her medications might be the cause. Her low blood pressure, as well as lorazepam, might be contributing. When you mention the latter, she says no one has ever told her that sleeping pills might cause confusion. She tried to stop them once, but had trouble sleeping so she just kept taking them. You explain the natural history of rebound insomnia and that it improves within days of stopping. She's willing to try again and agrees to taper the dose. You call to update the family physician about this plan. You also discuss using a higher blood pressure target range, especially in light of her hypotension and dizziness. Her physician agrees to begin tapering doses of her antihypertensives. With the agreement of the patient and family physician, you email a lorazepam and antihypertensive tapering plan to her son, with a handout of withdrawal reactions to expect and information on an appropriate blood pressure target range.

STEP 4 SIMPLIFY TO REDUCE PILL BURDEN

Pill burden usually refers to the total number of pills or doses a patient must swallow during the day. Mrs. Archibald's original 17 medications carried a pill burden of 36 tablets or capsules daily. Complex regimens and poor timing or unnecessary separation of multiple medications can lead to errors in medication administration; they may also affect quality of life, as patients feel they cannot vary from their strict regimen and sometimes feel too full of medication to eat. Patients may complicate high pill burden regimens by creating more complex dosage schedules (eg, 7 times a day instead of qid), especially when medication instructions in wording (eg, twice daily vs every 12 hours).⁶⁰ Stopping or tapering unnecessary medications decreases the potential for adverse drug events and interactions also reduces pill burden, which simplifies medication scheduling.

Once unnecessary and side-effect causing medications have been stopped, steps further to reduce pill burden and enhance adherence include using combination (eg, diuretic + another antihypertensive-lowering drug + two hypoglycemics) or from multiple-times-daily to formulations.^{61,62}

By checking with Mrs. Archibald every few weeks and working closely with her doctor, your patient has been able to significantly reduce her pill burden. By combining several you've reduced her number of to 9 and her pill burden to 16, taken twice daily instead of four times with only one blister pack! She is feeling much better, eating normally, and has started out again to her various activities.

Conclusion

Polypharmacy is a growing problem in scope and impact. By 2036, one in four Canadians will be older than 65 years of age; this growing demographic is at risk for drug therapy problems.⁽⁶³⁾ With recent regulatory and reimbursement changes, pharmacists are even more well-placed to actively participate in optimizing therapy in the elderly. Helpful resources to assist pharmacists in individualizing therapy and reducing polypharmacy in the elderly are presented in Table 6. Pharmacists must share responsibility with prescribers and patients to ensure that potentially inappropriate medications are minimized, appropriate medications and doses are used, side effects are not treated with more medication without first investigating medication-related causes, and pill burden is minimized.

References and tables 1, 3, 4, 5, and 6 are available at www.CanadianHealthcareNetwork.ca. Click on the Pharmacy Practice logo to view archives.

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