

Polypharmacy and prescribing cascades

Medicine use is the most common intervention in health care. Polypharmacy is common in residential aged care. However, older persons are particularly vulnerable to adverse events associated with medications. Aging is associated with numerous physiological changes that affect how medicines are absorbed, distributed, metabolised and excreted. These changes increase the risk of adverse events and medicine-related harm.

Quality use of medicine and medicine safety is a National Health Priority. The World Health Organization (WHO) launched its Medication Without Harm initiative in 2017, which aimed to reduce medicine-related harm by 50% within 5 years. The National Aged Care Mandatory Quality Indicator (QI) Program requires collection of data on polypharmacy. For the purposes of the QI Program, polypharmacy is defined as the prescription of nine or more medications. The reported prevalence of polypharmacy in residential aged care facilities ranges from 12.8% to 74.4%.

Inappropriate polypharmacy

Over 95% of people living in residential aged care have at least one problem with their medicines; and most have three problems. One in six medicine-related problems are due to adverse medicine reactions. It is estimated that more than half of adverse events could be prevented with safer prescribing practices and regular medication reviews.

Common problems associated with polypharmacy include:

- Falls and fractures
- Dehydration
- Functional decline
- Cognitive impairment
- Delirium
- Declining nutritional status
- Drug interactions
- Hospitalisation

There are many lists of potentially inappropriate medicines (PIMs) in older persons. PIMs are medicines that are known to be potentially harmful when used by older adults, where the potential risk of harm outweighs the anticipated benefit, particularly when safer or more effective alternatives for the same condition are available. Over half of all people living in aged care facilities are prescribed medicines that are considered potentially inappropriate in older people.

Potentially suboptimal regimens often include medications with anticholinergic and sedative properties. There is some evidence that older people prescribed one or more PIMs have an increased probability of death. PIMs are also linked to an increased risk of hospitalisation and emergency department visits. There is also some evidence linking the use of PIMs with an increased risk of falls and fractures.

Prescribing cascades

Prescribing cascade describes the use of medicines to treat the adverse reactions of another medicine, misinterpreted as a new medical condition requiring treatment. Prescribing cascades are relatively common among older persons. This is due in part to polypharmacy.

Some examples of prescribing cascades include:

- Cholinesterase inhibitors → urinary incontinence → anticholinergic medication
- NSAID → hypertension → antihypertensive medication
- NSAID → stomach ulcers → PPIs
- NSAID → PPI prophylaxis → vitamin B12
- Thiazide diuretics → gout → allopurinol
- Metoclopramide → Parkinsonian symptoms → antiparkinsonian medication
- Antipsychotics → Parkinsonian symptoms → antiparkinsonian medication
- Gabapentin → peripheral oedema → diuretics
- Calcium channel blocker → peripheral oedema → diuretics
- ACE inhibitor → dry cough → antitussives

One of the most commonly reported prescribing cascades is calcium channel blocker (CCB)-induced peripheral oedema. The peripheral oedema associated with CCBs is not caused by fluid overload or retention, but by fluid redistribution. Consequently, diuretic treatment is not necessary or useful, and increases the risk of adverse events including falls, urinary incontinence, electrolyte disturbances and kidney injury.

Anticholinergic-PPI prescribing cascade

A prescribing cascade of proton pump inhibitors (PPIs) following anticholinergic medications in older people with dementia was recently described. Studies have shown about 50% of people with dementia are taking medicines with anticholinergic properties.

PPIs (esomeprazole, lansoprazole, omeprazole, pantoprazole, rabeprazole) are widely prescribed for a variety of stomach-related conditions (peptic ulcer disease, gastro-oesophageal reflux disease, ulcer and upper gastrointestinal bleeding prophylaxis) and dyspepsia symptoms. Studies have shown a significantly higher prevalence of inappropriate PPI use in people with mild cognitive impairment (MCI) and dementia. Numerous adverse effects have been identified, especially with long-term use. These include increased fractures, *Clostridium difficile* infections, disruption of the gut microbiome, electrolyte disturbances and increased risk of pneumonia.

Medications with anticholinergic properties include antihistamines, antidepressants, antipsychotics, and bladder anticholinergics. Some examples commonly used in residential aged care include risperidone, quetiapine, and amitriptyline. These medications are highly anticholinergic. Some herbal preparations also have anticholinergic properties, e.g. knotweed.

Classic anticholinergic side effects include dry mouth, blurred vision, impaired sweating, confusion, decreased lower oesophageal sphincter tone, constipation and urinary retention. More concerning among older people is the association with an increased risk of falls, delirium, dementia and poorer outcomes in those with dementia. In addition, medications with anticholinergic properties antagonise cholinesterase inhibitors used in the management of dementia (donepezil, rivastigmine, galantamine); so this combination should always be avoided.

It has been proposed that anticholinergic-induced gastrointestinal adverse events may be misinterpreted as new symptoms of gastro-oesophageal reflux, with subsequent prescription of a PPI. This may be especially problematic as people with dementia may have impaired ability to explain their symptoms or remember when symptoms started.

Prevention

When a resident presents with new symptoms, the potential for these new symptoms to be caused by an existing medication should be considered, particularly if the medication has been recently started or the dose increased. The decision to prescribe a second medicine to counteract an adverse drug reaction from a first medicine should only occur after careful consideration, and where the benefits of continuing therapy with the first medicine outweigh the risk of harm of additional adverse reactions from the second medicine and contribution to polypharmacy.

Avoiding prescription of potent anticholinergic medications for people living with dementia is likely to be most successful for reducing complications associated with anticholinergic medication use like the prescribing cascade detailed in this article. If anticholinergics are deemed necessary, early identification of adverse reactions is necessary to avoid the anticholinergic-PPI prescribing cascade.

PPIs should be reduced slowly by lowering the dose every one to two weeks to avoid rebound symptoms. In general, anticholinergics should be gradually reduced by 25-50% of the daily dose every 1-4 weeks. Anticholinergic withdrawal symptoms can occur within 1-3 days. They include irritability, anxiety, insomnia, sweating and gastrointestinal effects; and can last up to 6-8 weeks.

Residential Medication management Reviews (RMMRs) have been shown to reduce anticholinergic medications and proton pump inhibitors in residential aged care.

References

- Medicine safety: aged care. Canberra: PSA; 2020.*
- Therapeutic Advances in Drug Safety 2022;13:1-41.*
- Frontiers in Pharmacology 2022;13:878092.*
- BMC Geriatrics 2020;20:368.*
- JAMA Intern Med 2020;180:643-651.*
- BMC Geriatrics 2022;22:493.*

➤ **The Webstercare Consultant Pharmacist Continuing Education Series** comes to you each month from your pharmacist. If you would like extra copies please visit www.webstercare.com.au or ask your pharmacist.