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EDITORIAL

Prescribing in the elderly

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Medicines can prolong life, relieve suffering and maintain dignity, but they can also harm. In South Africa, where primary care is often the first point of call for the elderly, the responsibility to prescribe wisely is a clinical imperative. However, prescribing for this demographic can be challenging. Significant heterogeneity with altered and variable pharmacokinetics and pharmacodynamics make this population uniquely vulnerable, while polypharmacy magnifies the risks of adverse drug reactions, interactions and prescribing cascades. These can be mitigated by intentional evidence-based prescribing, regular review, judicious deprescribing, shared decision-making and multidisciplinary collaboration.

Keywords: elderly, polypharmacy, adverse drug reactions, prescribing cascades, deprescribing

Introduction

South Africa, like much of the world, is experiencing a demographic shift towards an aging population. The World Health Organization estimates that by 2030, one in six people globally will be over the age of 60, and our country is not immune to this trend. By 2050, 80% of older people will be living in low- to middle-income countries.[1] For general practitioners (GPs), this is especially relevant because the elderly (> 65 years) are likely to present with multiple chronic illnesses, necessitating the prescription of more medicines than any other age group. Multimorbidity is strongly associated with polypharmacy, often defined as the concurrent use of five or more drugs.[2,3] Besides multimorbidity informing polypharmacy, almost half of older adults take one or more unnecessary medications, which exposes them to often unexpected risks. The definition of polypharmacy may therefore be expanded to encompass medications that are unnecessary, ineffective or represent therapeutic duplication.[2]

Prescribing in the elderly is more nuanced than aligning treatment with disease-focussed guidelines or avoiding polypharmacy. It is in some respects unfortunate that as we age, we become increasingly dissimilar, requiring bespoke approaches. There is enormous variability in our physical and cognitive fitness, frailty, homeostatic reserve, comorbidity, nutritional status, gut microbiota and life-expectancy.[4] All of these factors are highly relevant for treatment and should be considered for individualising treatment. The aging process also affects major organs and therefore drug absorption, distribution, metabolism and excretion. Pharmacodynamic responses are altered too - often exaggerated - making older patients more sensitive to both therapeutic effects and to adverse drug reactions (ADRs).[4,5] The result is a prescribing landscape in which vulnerability to drug-drug and drug-disease interactions, hospitalisation and functional decline is ever-present.

The familiar adage of "start low and go slow" in the elderly reflects known changes in pharmacokinetics and pharmacodynamics that occur with aging.[4,5] It must be noted, though, that few drugs have been formally tested in this population, creating abundant research opportunities to bridge this knowledge gap. Available evidence suggests that the extent of drug absorption is usually preserved, but slower gastrointestinal transit and reduced splanchnic blood flow may delay onset of drug action. Distribution is significantly affected by body composition. Reduced lean body mass and total body water associated with the aging process raise plasma concentrations of hydrophilic drugs (aminoglycosides, digoxin), while increased fat stores serve as reservoirs that prolong the half-life of lipophilic agents such as those affecting the central nervous system (benzodiazepines, antidepressants). Liver mass and blood flow are reduced, compromising the clearance of drugs such as glyceryl trinitrate.[5] Hepatic metabolic capacity is also diminished, particularly phase I oxidative reactions, which mostly rely on cytochrome P450 enzymes. This predisposes to accumulation of drugs metabolised by this route, whereas phase II conjugation pathways are relatively spared.[6] Renal excretion is particularly compromised as glomerular filtration rate declines with age. Typically, people lose nephrons and therefore kidney function by about 1% a year after age 50, sometimes in the absence of elevated serum creatinine, which may appear deceptively normal due to reduced muscle mass.[7,8] Consequently, renally cleared drugs with narrow therapeutic indices such as digoxin, lithium and aminoglycosides, require careful dose adjustment.[6-8]

Pharmacodynamic changes add an extra layer of complexity. For instance, elderly patients may be more sensitive to warfarin's anticoagulant effects, or experience exaggerated analgesic and sedative effects of opioids and benzodiazepines, respectively,[5] and greater hypotensive responses to antihypertensives and susceptibility to the anticholinergic aspects of many medicines. In fact ADRs account for around 10% of hospital admissions in the elderly, with NSAIDs (upper gastrointestinal bleeding, hypertension, major adverse cardiovascular events and kidney failure) at the top of the list, followed by beta-

blockers, antibiotics, oral anticoagulants, digoxin, ACE inhibitors, calcium channel blockers, chemotherapy, opioids and oral antidiabetic agents.[9] The interplay of altered pharmacokinetics and pharmacodynamics means that standard doses are often inappropriate and vigilance is essential.[10] Higher targets such as relaxed systolic pressure thresholds or individualised HbA1c are often appropriate to balance efficacy with safety; likewise, in patients on digoxin, close clinical monitoring of renal function as well as hypokalaemia could prevent ADR-related hospitalisation.[8,9] These susceptibilities in older adults are compounded by polypharmacy, which amplifies the risks of ADRs, drug-drug and drug-disease interactions, and prescribing cascades.

For some, polypharmacy is the rational outcome of multimorbidity and evidence-based treatment guidelines. For others, it arises from fragmented care, duplication of therapy, poor communication between prescribers and unsupervised use of over-the-counter or complementary medicines. Regardless of the cause, the consequences may be serious. The likelihood of drug-drug interactions rises disproportionately with each added prescription. Sedatives and antihypertensives contribute to falls and fractures, which are a leading cause of morbidity and mortality in older adults.[11,12] Complicated regimens undermine medication adherence, especially in patients with cognitive impairment, while prescribing cascades, where an adverse drug effect is mistaken for a new condition and treated with yet another drug, drive the cycle of overmedication.[13,14] Polypharmacy is not always inappropriate, but it should always be intentional. All prescriptions require regular critical evaluation of indication, benefit, safety and alignment with the patient's care goals. The patient's voice is important. Shared decision-making ensures that treatment reflects patient ambitions, whether longevity, symptom relief or preserving independence.[15,16]

Lessons from clinical practice

The intricacies of prescribing in the elderly are best illustrated through clinical scenarios. One striking example involved an 81-year-old man who presented with hallucinations and epistaxis. He had long been maintained on warfarin for atrial fibrillation, but after hearing a radio programme, he independently added daily aspirin. To this regimen, a GP prescribed cimetidine for heartburn. The combination was toxic. Aspirin added both a pharmacodynamic and pharmacokinetic bleeding risk to warfarin, cimetidine inhibited hepatic metabolism which further raised his INR, and the hallucinations were attributable to cimetidine itself. This case highlights the dangers of self-medication, poor coordination between prescribers and lack of over-the-counter histories. The appropriate course was to discontinue unnecessary drugs, reinforce the importance of avoiding unsupervised medicines and monitor anticoagulation more closely.[4]

Another case concerned a 75-year-old with hypertension and heart failure, already receiving an ACE-inhibitor, who was prescribed ibuprofen for acute back pain. From an orthopaedic standpoint, the analgesic was reasonable, yet it posed significant risks from a cardiac perspective. NSAIDs may cause fluid retention, exacerbate heart failure and increase cardiovascular and gastrointestinal morbidity.[17] Drug interactions with ACE-inhibitors include hyperkalaemia and increased risks of renal impairment. Alternatives included optimising paracetamol, a short course of tramadol, topical diclofenac and referral to physiotherapy. Here the lesson was clear: what benefits one organ system may imperil another, and the GP may be the only clinician positioned to weigh these competing risks.

A third scenario highlighted the danger of inappropriate and extended drug continuation. An 86-year-old nursing home resident remained on warfarin two years after hip surgery, well beyond the recommended prophylactic period. The oversight reflected shared responsibility: prescribers had failed to discontinue the anticoagulant, facility staff had not questioned its necessity and pharmacists had not intervened. The patient remained on a high-risk therapy without indication, exposing him to bleeding risks that outweighed any theoretical benefit.[18] Every drug should be initiated with a stop date in mind, particularly when used for prophylaxis.

Finally, there was the case of an 84-year-old man discharged from hospital on no fewer than 17 drugs. Many were duplicates or unnecessary. Through careful reconciliation, his therapy was rationalised: tramadol and omeprazole were withdrawn, aspirin and atorvastatin were reduced to lower doses and other medicines were adjusted. The result was a more manageable regimen and a safer therapeutic profile. This example stresses the value of systematic medication review and the courage required to deprescribe.

Across these hypothetical cases, several pitfalls become apparent. Over-the-counter and complementary medicines are frequently overlooked, yet can cause serious interactions. Medications are often continued long after the indication has lapsed. Duplication of drug classes creeps in, particularly in patients under the care of multiple specialists. High-risk agents such as benzodiazepines, sedating antihistamines, anticholinergics and NSAIDs are too often prescribed without consideration of safer alternatives. And there is a tendency to forget to align prescribing with patient priorities, such as maintaining independence, reducing pill burden or simply enjoying better quality of life.

Safer prescribing in the elderly is not achieved by any single measure but through a constellation of good practices. Medication reconciliation at every transition of care is essential, ensuring that the full drug list, including over-the-counter and complementary products, is accounted for.[19] Tools such as the Beers Criteria[20] and the STOPP/START framework[21] can guide clinicians in identifying potentially inappropriate prescriptions and facilitate medication review. Deprescribing, once a neglected area, is now recognised as an important component of rational care, requiring the cautious tapering and discontinuation of drugs that no longer provide benefit or posef disproportionate risk.[22,23]

Specialists often prescribe within the narrow confines of their own discipline, but GPs integrate and reconcile across conditions.

The GP must embrace collaboration. Non-pharmacological strategies such as physiotherapy, exercise, dietary modification and psychosocial interventions should also be considered wherever possible. Pharmacists, nurses and allied professionals all contribute to safer prescribing, and team-based approaches consistently improve outcomes.

While polypharmacy is not inherently inappropriate, the question is whether or not it is rational, monitored and patient-centred. In frail elderly patients, reducing medication burden can improve adherence, lower the risk of ADRs and enhance quality of life. Yet under-treatment should also be avoided. Proven therapies such as ACE inhibitors in heart failure remain effective even in advanced age, and should not be withheld simply because of chronological age. Rather, one should proceed carefully.[24] The art of prescribing in the elderly therefore lies in negotiating this delicate balance, and in the end, what matters most is not how many drugs an older patient takes, but if each one still earns its place in their life.

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