

Deprescribing: Less is More for Elderly Patients?

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A CASE VIGNETTE

A 77-year-old man has been attending Medical Clinic for hypertension, hyperlipidaemia, atrial fibrillation, recurrent strokes (first ischaemic at age 71 years, second haemorrhagic at age 73 years), dementia, and chronic kidney disease. His medications prescribed in his last clinic visit half year ago include Aricept (donepezil), betaloc, citalopram, edoxaban, lactulose, melatonin, pepcidine, thiamine and Zocor (simvastatin).

His wife and son brought him to attend a Geriatric Clinic because he was noted to have significant cognitive and functional deterioration for the past one month, with two episodes of falls, and intermittent urinary and faecal incontinence requiring the use of napkins, causing significant caregiver stress on the family.

Would you stop any of his drugs? Which ones? Why?

INTRODUCTION

The word "poison" was the collective term for all medicines in early Chinese history, alerting the healer of their cautious and appropriate use. Elderly patients are especially prone to drug-induced illness, as they differ from younger adults in terms of comorbidity, polypharmacy, pharmacokinetics and greater vulnerability to adverse drug reactions (ADRs).¹ The potential impact of medications in threatening the functional independence of an elderly person has long been recognised in Brocklehurst's frailty balance of breakdown in old age,^{2,3} and recently "medications" have been framed into the geriatric 5Ms^{4,5} (Table 1) as the need to consider medication burden in the holistic care of elderly patients. Hospitalised elderly patients are two to three times more likely to experience an ADR than patients aged 20 to 30 years,⁶ and 16% experienced significant ADRs.⁷ One in three elderly persons in primary care uses potentially unnecessary or inappropriate medications⁸ that can increase their risk of ADR,⁸ hospitalisation,⁹ death,¹⁰ and worsening geriatric syndromes.^{11,12}

ADRs in old age frequently remain unrecognised by doctors or patients, and often masquerade as the geriatric syndromes of instability (falls, faints), intellectual impairment (delirium, dementia), incontinence, immobility, and failure to thrive.^{11,12} Despite their impact on elderly patients and their caregivers, these geriatric syndromes are often ignored (the inverse care law), and their presenting problems are managed instead as diseases under multiple specialties,

triggering unnecessary investigations and further drug prescriptions (prescribing cascade). All these would have been avoided if the geriatric syndromes were identified early as drug-induced and the implicated drugs reduced or stopped.

Deprescribing refers to the planned discontinuation or dose reduction, under medical supervision, of medication when the benefits of continued use or at the current dose no longer outweigh the risks.¹³ Deprescribing encompasses the process of medication review and optimisation, and is an essential component in the 5Ms of age-friendly care to improve the quality and safety of care of elderly patients.¹⁴

Table 1. The geriatrics 5Ms and their relevant factors to consider in the holistic care of elderly patients (Adapted from references 4 and 5)

Geriatrics 5Ms	Relevant factors
1. Matters most to me	individualised preferences and goals
2. Mind	cognition and mood
3. Mobility	dexterity, swallowing, life space, fall risk
4. Medications	medication burden, drug-induced geriatric syndromes, polypharmacy, prescribing cascades
5. Multi-complexity	multi-morbidities, medical and social, ethical and legal

CLINICAL PRACTICE OF DEPRESCRIBING

Tools

Practical tools, based on consensus building from updated literature, have been designed to optimise the deprescribing process, e.g. Beers Criteria for potentially inappropriate medication (PIM) use in older adults;¹⁵ the screening tool of older people's prescriptions and screening tool to alert to right treatment (STOPP/START) criteria;¹⁶ Screening Tool of Older Persons Prescriptions in older adults with high fall risk (STOPPFall);¹⁷ and The Screening Tool of Older Persons Prescriptions in Frail adults with limited life expectancy (STOPPFrail).¹⁸ However, a simple list of explicit prescribing criteria or PIM cannot replace personalised clinical care of an elderly patient that requires time and skill.



Medication Review and Deprescribing

Medication review is a common practice to address inappropriate polypharmacy. It is a systematic examination of a patient's medicines against his/her diagnoses and problem list, with the purpose of augmenting the impact of medicines, reducing the number of medication-related complications, and decreasing waste.¹⁹ A structured multidisciplinary medication review by physician, pharmacist and nurse has been shown to reduce inappropriate psychotropic drug prescriptions for neuropsychiatric symptoms in nursing home patients with dementia.²⁰ Meta-analyses of the few randomised controlled studies on medication reviews and deprescribing in community-dwelling and frail elderly persons have shown reduction of PIM, total number of medications per patient, and mortality, but the impact on clinical outcomes (depression, cognition, falls, function and frailty) are variable, and there is insufficient evidence in terms of quality of life, frailty score and hospital admissions.²¹⁻²³ However, this has to be offset against the complete lack of evidence that additional medications in elderly people with frailty is beneficial, viz: whether adding the eleventh tablet has the same beneficial effect, similar to the other ten, when compared to trials recruiting an idealised, non-frail trial population.

The current body of evidence yields little guidance for practitioners on exactly how to deprescribe. A 5-step deprescribing protocol has been proposed²⁴:

1. Ascertain all drugs the patient is currently taking and the reasons for each one
2. Consider the overall risk of drug-induced harm in individual patients in determining the required intensity of deprescribing intervention
3. Assess each drug in regard to its current or future benefit potential compared with current or future harm or burden potential
4. Prioritise drugs for discontinuation that have the lowest benefit-harm ratio and lowest likelihood of adverse withdrawal reactions or disease rebound syndromes
5. Implement a discontinuation regimen and monitor patients closely for improvement in outcomes or onset of adverse effects.

Deprescribing may be in response to a significant event such as functional change, ADR, hospitalisation or residential care home admission. It may be proactive in a clinical encounter of patients with inappropriate polypharmacy, part of an advance care planning process, or part of end-of-life care.²⁵ Appropriate prescriptions and deprescriptions at the "right time" and of the "right medications" for frailer elderly persons aren't always clearcut, because they are often underrepresented in randomised trials and evidence-based medicine.²⁶ Disease-specific guidelines, based on risk-benefit studies on the use of a single drug for a single disease simply cannot be extrapolated to the clinical care of an elderly person with multiple diseases on multiple drugs. Given the uncertainty of deprescribing and prescribing in frail elderly people, it is helpful to adopt a multidisciplinary

shared decision making approach that respects individual goals and priorities. Deprescribing requires a thoughtful explanation to patients and caregivers. Deprescribing is not about restricting the access to healthcare (less care) but instead an acceptance of the limitations of drugs, especially in complex frail elderly patients. While patients may have symptom reversal for drug-induced problems, they need to accept the risk of withdrawal effects, which necessitates monitoring and follow up. Also, multiple aetiologies commonly occur in old age. Thus, initial resolution of symptoms upon drug withdrawal with later recurrence of similar symptoms may indicate an underlying disease sharing similar presentations as ADR, illustrated by a case report of a patient with both timolol-induced bradycardia and atrio-ventricular conduction defect.²⁷

Hurdles

Different barriers were identified that impede the implementation of deprescribing.^{25,28-33} Cultural and organisational barriers included a culture of diagnosing and prescribing; evidence-based guidelines focused on single diseases; a lack of evidence-based guidance for the care of older people with multimorbidities; limited incentives for deprescribing, and a lack of collaborative working, shared communication, interoperable electronic health records, decision-making systems, tools, and resources. Interpersonal and individual-level barriers included professional etiquette; clinician time constraints, fragmented care; lack of information for a full clinical picture of the patient; lack of confidence to deprescribe and fear of negative consequences; prescribers' and patients' strong belief in the continuation of medicines; prescribers' and patients' uncertainties and lack of knowledge; and gaps in tailored support.

Tallis, recognising the information overload confronting clinicians dealing with the increasingly complex medical problems of an ageing population, advocated back in 1986 the use of information technology to assist the prescriber to help control the present epidemic of drug-induced disease.³⁴ Initial success in reducing PIM in hospitalised elderly patients was shown in a systematic review examining the impact of computerised clinical decision support systems (CDSS).³⁵ However, the subsequent international SENATOR RCT, a CDSS based on the STOPP/START criteria, was introduced without success.³⁶ The failure of the implementation of SENATOR software-generated medication advice was attributed to limited engagement due to lack of knowledge, uncertainty of the effect and time pressures.

The hurdles of deprescribing can be overcome by education and training on proactive deprescribing; prudent prescribing; greater availability and acceptability of non-drug alternatives; resources; improved physician-patient and physician-physician communication, collaboration, knowledge, and understanding; and shared decision-making.^{28-31,37,38} To facilitate safe deprescribing, a whole system, patient-centred approach is required, involving good communication and relationships among key decision-makers, healthcare professionals, patients, and caregivers, supported by improved healthcare informatics.^{5,28-31}

It has been advocated that with the geriatrics 5Ms (Table 1) holistic approach and appropriate support, prescribers in partnership with their patients and care team can be better equipped to optimise polypharmacy to support what matters most to our elderly patients.⁵ In a scoping review of deprescribing intervention trials, clear consideration of "Medication" was noted in deprescribing trials, as expected. However, "Mind", "Mobility", and "What Matters Most" have been considered to varying degrees in deprescribing trials, limiting the potential of deprescribing evidence to contribute to improvements in comprehensive geriatric clinical care.¹⁴ It has been proposed that future deprescribing interventions and practices that incorporate patient-centeredness in the design and outcome assessment are needed to promote the age-friendliness in deprescribing.¹⁴

CONCLUSION AND ADVICE

Deprescribing is the art of appropriate prescription with knowledge of the elderly person in context, balancing the harmful and beneficial effects of medications, while acknowledging the limitation of evidence-based medicine and disease-specific guidelines. The frailty balance³ is modified (Fig. 1) to show the dual nature of medications, medications as disease simulators, and the role of non-drug measures in enhancing physical and mental health. The dynamic nature of the frailty balance reminds us that ill health in old age can be reversed by restoring the equilibrium through attending to its positive and negative factors: deprescribe or prescribe appropriately in context, enhancing physical and mental health with non-drug measures, enhancing social support, and accurate diagnosis and treatment of diseases, while recognising that diseases in old age can often be drug-induced, and the treatment then is drug withdrawal instead of adding more drugs.

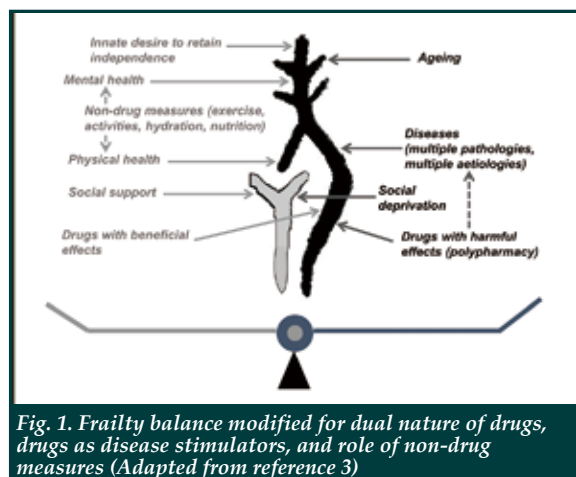


Fig. 1. Frailty balance modified for dual nature of drugs, drugs as disease stimulators, and role of non-drug measures (Adapted from reference 3)

"Less (drugs through deprescription) is more (effective)" has been demonstrated in studies in reducing PIM and polypharmacy in elderly populations, but not consistently for other clinical outcomes. Yet, deprescription is recommended for elderly patients, especially frailer ones, because of the high prevalence of inappropriate polypharmacy among them and the consequent harmful effects. For the individual elderly

person: "less is more" if the person is inappropriately overprescribed with consequent harmful effects to be managed by deprescription; "less is less" if the person is a victim of missed treatment opportunity and underprescribed for a condition that will benefit from appropriate prescription. In clinical practice, this boils down to medication review, looking at the whole person, appropriate prescription/deprescription in context, and discussion on goals of care during a clinical encounter of an individual elderly patient.

Returning to the case vignette, medication review with the patient's son, who supervised his medication taking, showed that the patient had been taking his prescribed drugs regularly except melatonin, lactulose, citalopram and donepezil, the last two being newly prescribed half year ago. His son had initially withheld citalopram and donepezil from his father for fear of side-effects mentioned in an internet search until two months ago, when a psychiatrist advised his son to start his father on citalopram for irritability and a hot temper. A month later, the patient was noted to be mentally slow with worsened cognition, and was brought to see a neurologist, who advised stopping citalopram and starting donepezil.

The patient's new onset of urinary and faecal incontinence, which resulted in breakdown of his independence stressing on his family, was likely precipitated by the cholinergic side-effect of donepezil,³⁹⁻⁴¹ and predisposed by his reduced walking speed after strokes. His recent instability and falls were secondary to postural hypotension due to dehydration (reflected by a high urea/creatinine ratio and haemoconcentration) and bradycardia; the former from deliberate self-restriction of fluid intake to avoid urinary incontinence; while the latter from the additive cholinergic side-effect of donepezil and beta-blocking effect of betaloc. Postural hypotension could also reduce his cerebral perfusion and worsen his cognition. His cognitive decline soon after the use of citalopram was likely related to the anticholinergic action of citalopram.⁴² Since donepezil use had been brief (one month) and at a low dose (5mg daily), the patient was advised to stop the culprit drug donepezil without any concern on withdrawal problem. He was also advised to take liberal fluid intake, and this together with stopping donepezil, would help minimise postural hypotension and fall risk, and enhance perfusion to his brain and kidneys. He had made sufficient recovery from his previous two strokes in his physical and cognitive function to independence in stick walking and activities of daily living, and his innate desire to retain independence supported the continuation of anticoagulation to prevent another stroke. Anticoagulation also helps to reduce the risk of atrial fibrillation-related cognitive decline.⁴³ The advice to him above helped to improve the benefit (stroke and dementia risk reduction in atrial fibrillation) to risk (bleeding) ratio of anticoagulant use through reducing fall risk from postural hypotension and bleeding risk from anticoagulant excess secondary to reduced renal clearance. Bleeding risk may further be reduced by changing to another anticoagulant less dependent on renal clearance for its elimination (e.g. apixaban) and using a dose adjusted for renal function. Home blood pressure monitor was advised to guide optimal treatment of his hypertension without



aggravating postural hypotension from zealous anti-hypertensive treatment. Counselling was given to his family on viewing challenging behaviours from the patient's perspective: as a mode of communication of unmet needs to be met by appropriate positive behaviour support.⁴⁴ Cognitive stimulation activities (6 Arts games, <https://www.eng.hkada.org.hk/>) were introduced to the patient and his family. The patient and his family were reassured that his recent physical and mental functional decline was likely drug-related and potentially reversible with drug withdrawal and hydration. The patient would be reviewed in one month, when a correspondence letter would be written to the Medical Clinic to update his condition and the medication optimisation made.

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