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Deprescribing

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Summary

Medicines have adverse effects and the use of multiple medicines, polypharmacy, can be associated with poorer outcomes. Health professionals need to recognise when medicines should be ceased and how to deprescribe. Deprescribing could be considered when there is polypharmacy, adverse drug reactions, ineffective treatment, falls or when treatment goals have changed. If patients are slowly weaned off their medicines, withdrawal and rebound syndromes are usually not serious. A cautious approach to deprescribing includes two principles – stop one drug at a time and wean doses slowly over weeks and months.

Key words: drug withdrawal, falls, polypharmacy.

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Introduction

There are many evidence-based guidelines to help clinicians start drug treatment. There is much less evidence to guide clinicians about withdrawing medicines. Several terms have been used for ceasing medicines including deprescribing, withdrawal, discontinuation, pharmacolysis, untrials and prescription pruning. Here deprescribing is used to define the cessation of long-term therapy, supervised by a clinician.

When should deprescribing be considered?

Good practice requires a regular review of a patient's medicines. These reviews are a good time to consider deprescribing.

Polypharmacy

The use of multiple medicines is termed polypharmacy. In older people it is associated with an increased risk of impaired physical and cognitive function, institutionalisation, hospitalisation and death. These associations appear to be independent of the underlying diseases.[1] Moreover, studies show that reducing the number of drugs has positive outcomes in older people. A feasibility study to reduce polypharmacy in people over 70 years of age suggested that over half of their medicines could be discontinued. Only 2% of the drugs needed to be restarted because the original indication re-emerged. Overall there was improvement in cognition and the patients' global health.[2] A review of medicine withdrawal studies in older people found that withdrawal was rarely associated with adverse effects.[3] After withdrawal of antihypertensive therapy, many patients (20–85%) remained normotensive and withdrawal of psychotropic drugs was associated with a reduction in falls and improved cognition.[3] This is further supported by a recent Australian pilot study which confirmed the feasibility of deprescribing in polypharmacy.[4]

Adverse drug reactions

It is common sense to stop a drug, or to reconsider its benefit:harm ratio, if it causes a significant adverse reaction. For example, in secondary stroke prevention trials of antiplatelet drugs, up to one in five patients stopped treatment because of adverse drug reactions. Given that clinical trial participants do not always reflect real-life patients, it is likely that a greater number of patients in everyday practice will be unable to tolerate their medicines. Health professionals often have difficulty recognising adverse drug reactions, partly because they are reluctant and unwilling to recognise them and partly because the reactions can be mistaken for symptoms of disease. Falls and cognitive impairment are frequently secondary to adverse drug reactions in older people, yet are often overlooked as simply part of the ageing process.[5]

Lack of effectiveness

For many drugs it is not possible for any individual clinician to assess effectiveness. This is because many drugs are used to prevent illness or because the number of patients who need to be treated for one to benefit is too large for the effect to be perceptible.[6] However, if a drug has no effect on a surrogate outcome (for example blood pressure, cholesterol) or symptoms, then it is pointless to continue therapy because it accrues cost and the risk of harm without any benefit.

Falls

Polypharmacy and drugs acting on the central nervous system are important risk factors for falls, increasing the risk by around 50%.[7] A placebo-controlled clinical trial of withdrawing psychotropic drugs showed that falls were reduced by 66%.[8] The number of hip fractures in Australia could be reduced by 10% simply by avoiding the use of benzodiazepines in older people.[9]

The relationship between cardiovascular drugs and falls is less clear. Antihypertensive drugs are often ceased in older people with orthostatic hypotension and recurrent falls.

Terminal illness, dementia or frailty

It is important to re-evaluate the role of medicines once a patient has entered the terminal phases of an illness, become frail or developed disabling dementia, as there should be a shift in treatment goals. Many preventive therapies such as medicines used to treat hypertension, osteoporosis and hyperlipidaemia take many months and even years before their benefit is established. They have limited value in patients with a short life expectancy. Furthermore the pharmacokinetics and pharmacodynamics of many medicines change with frailty or terminal illness and this impacts on their harm:benefit ratio. Deprescribing will reduce the medicine load and potential adverse effects, while shifting the therapeutic focus to end-of-life issues that are important to the patient.[10]

What are the consequences of deprescribing?

Like all medical interventions, including starting medicines, there are potential harms and benefits in deprescribing. There are several possible outcomes following deprescribing.

No obvious change in clinical status

In many cases there may be no obvious change in the patient after deprescribing. However, patient satisfaction is often increased, the financial cost to the patient and the community is reduced and the risk of future adverse drug reactions and interactions is removed.

Resolution of specific adverse drug reactions

For dose-dependent adverse drug reactions, resolution of the adverse effect will usually coincide with the disappearance of the drug from the blood (3–5 half-lives). However, in some situations, such as delirium, resolution may take much longer than expected on pharmacokinetic grounds.

Improvement in function and quality of life

In a clinical trial to reduce polypharmacy in older people, the patients' global assessment scale improved in 88% and in most patients cognitive function improved.[2] A systematic review concluded that deprescribing can be associated with improvements in cognition and behaviour in patients with dementia, and a reduction in falls.[3] Simplification of drug regimens might also improve adherence and reduce medication errors.

Withdrawal syndromes

When deprescribing is undertaken slowly and under medical supervision, clinically significant adverse withdrawal reactions are rare.[2,3] Even so, clinicians should be aware of potential problems.

Withdrawal and discontinuation syndromes

The most common cause of discontinuation syndromes is the withdrawal of drugs acting on the central nervous system. Most general practitioners will be familiar with the antidepressant discontinuation syndrome commonly seen after ceasing selective serotonin reuptake inhibitors. The symptoms typically occur within one week of ceasing the drug. They are usually mild, and resolve over ten days or less. The abrupt withdrawal of benzodiazepines is associated with a much more serious withdrawal syndrome with confusion, hallucinations and seizures. Abrupt cessation of levodopa is associated with a serious withdrawal syndrome with features of the neuroleptic malignant syndrome, including severe muscle stiffness, autonomic instability and impaired consciousness. In patients who have been taking systemic corticosteroids for more than a few weeks, sudden cessation may sometimes lead to an Addisonian crisis secondary to suppression of the hypothalamic-pituitary-adrenal axis.[11,12]

Rebound syndromes

Stopping a beta blocker can be associated with rebound tachycardia and hypertension which may aggravate heart failure or ischaemic heart disease. Stopping proton pump inhibitors is associated with hypersecretion of acid and aggravation of gastrointestinal symptoms. Simple analgesics and nasal drops can be obtained without a prescription, but cessation can be respectively associated with rebound headaches and rhinorrhoea.[12] Rebound insomnia is common after stopping hypnotic drugs.

Unmasking drug interactions

Pharmacokinetic interactions should be considered when undertaking deprescribing. For example, if omeprazole is ceased by a patient on a stable dose of warfarin, the INR may decrease because omeprazole had been inhibiting the metabolism of warfarin.

Reappearance of symptoms of original disease or risk factor

It is important not to misinterpret a rebound or withdrawal syndrome as a recurrence of the symptoms of the original disease. Surprisingly, clinical trials of drug withdrawal do not

show a high incidence of symptoms of the original disease or risk factor reappearing after treatment stops.[3] However, if some drugs, for example immunosuppressants, are stopped abruptly the underlying condition may flare up.

What is the approach to deprescribing?

There is limited clinical evidence to guide deprescribing, but some broad principles can be applied (Fig. 1).[2,4,11,12]

Prepare the patient for deprescribing

When starting a drug, explain to the patient that the outcome will be monitored and the drug might be ceased if there is no beneficial effect or a significant adverse effect occurs. Patient expectations can be discussed and managed at this time. This is particularly important for drugs which have Pharmaceutical Benefits Scheme (PBS) continuation criteria (for example cholinesterase inhibitors for Alzheimer's disease), as the clinician must confirm that there has been clinical improvement in order for PBS funding to continue.

Recognise the need for deprescribing

The main clues that deprescribing might be useful are polypharmacy, adverse drug reactions (for example falls in older people), lack of efficacy and changes in treatment goals which may be secondary to the onset of terminal illness, dementia or frailty.

Prioritise medicines to cease or doses to reduce

A cautious approach is to stop or reduce the dose of one drug at a time. This helps to identify which drug might have been causing harm or, if withdrawal symptoms occur, to provide a guide for which drug to consider recommencing. If an adverse drug reaction is suspected, then the implicated drug should obviously be stopped first.

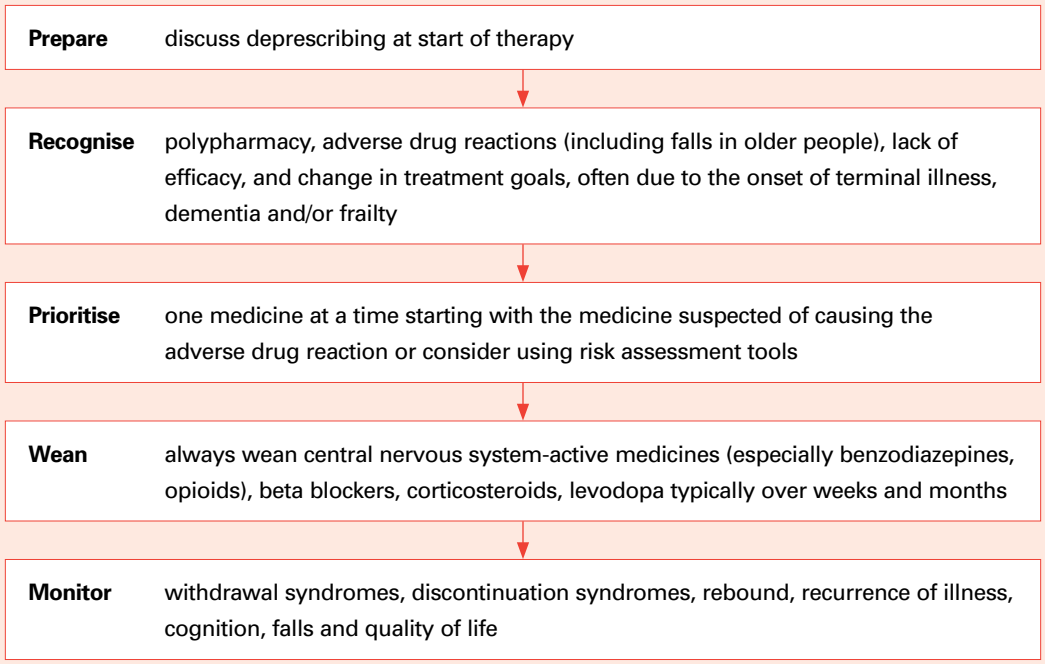
If the patient is elderly and taking multiple medicines then there are several possible approaches to identifying the drugs which are suitable for deprescribing, in particular focussing on anticholinergic and sedating drugs.[2,13,14] Reducing the dose of a medicine or changing it from regular to 'as needed' might also be an appropriate goal.

Wean or taper the dose

In many cases, medicines can be ceased abruptly, while for others (beta blockers, benzodiazepines, corticosteroids, opioids, levodopa) sudden cessation can generate serious withdrawal and rebound syndromes. The duration of weaning can vary from days to months and is influenced by factors such as the drug's half-life, the availability of different dose form sizes and scored tablets, as well as the physiological and psychological responses of the patient. For psychotropic medicines, the overall aim might be to reduce the dose by 25% each month, adjusting this according to the patient's response.[12,15,16] This

Fig. 1

General approach to deprescribing



is a reasonably conservative regimen that would be suitable for most other prescription drugs if there was concern about withdrawal or rebound. For patients who have taken benzodiazepines for a long time, there might also be a benefit in transferring the patient to an equivalent dose of diazepam, because of its long half-life, then commencing withdrawal. However, for patients who have had a serious adverse drug reaction, then usually the drug should be stopped immediately.

Monitor outcomes

If a significant withdrawal syndrome or rebound occurs, then the drug could be resumed. Withdrawal could be attempted later at a slower rate.

Assess patients for positive outcomes of deprescribing, such as decreased adverse effects and improved function. These benefits will be important for continuing compliance with deprescribing.

Conclusion

Recognising adverse outcomes or a lack of efficacy requires skill and diligence, particularly in older people taking multiple medications. However, good patient care depends upon the ability of prescribers to evaluate the clinical need for deprescribing and then undertake supervised withdrawal of medicines when appropriate.

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Conflict of interest: none declared

Self-test questions

The following statements are either true or false (answers on page 195)

7. Antihypertensive drugs are not suitable for deprescribing because of the risk of rebound hypertension.
8. Sudden cessation of long-term use of benzodiazepines may cause hallucinations.

RADAR
Rational Assessment of Drugs and Research

The December issue of NPS RADAR reviews the evidence and place in therapy for:

- asenapine (Saphris) for schizophrenia or bipolar 1 disorder (acute mania or maintenance)
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- ticagrelor (Brilanta), an oral antiplatet for acute coronary syndrome
- oxycodone-with-naloxone controlled-release tablets (Targin) for chronic severe pain.

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