Deprescribing Hypertension Medication in Older Adults

Can It Lower Drug Burden Without Causing Harm?

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KEYWORDS

• Hypertension • Deprescribing • Older people • Polypharmacy

KEY POINTS

- Antihypertensives are one of the groups of medications most used by older populations, and more intensive treatment goals may have potential for adverse events.
- When planned and patient-centered, antihypertensive deprescribing has not been associated with any significant adverse outcomes.
- Antihypertensives might benefit patients with comorbidities, and they may be prescribed with a specific focus on addressing these additional health concerns. Discontinuing such agents could exacerbate the underlying conditions for which they were initially prescribed.
- A medication review considering the prescription of inappropriate antihypertensives and their gradual withdrawal should be carried out.

INTRODUCTION

Drugs are the most commonly used medical technology to treat chronic diseases, and older patients often need to use multiple drugs due to multimorbidity.[1] The drug

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burden may increase hospitalization, cognitive impairment, falls, and increased mortality in this population.[1,2] The presence of multiple health conditions, leading to the use of multiple medications (polypharmacy), along with geriatric syndromes like cognitive decline and socio-economic challenges such as loneliness or lack of informal assistance, significantly affects the quality of life for older individuals and the standard of health care they receive.[3] The challenge is making decisions based not solely on age but on carefully considering the patient's overall medical, physical, social, and mental characteristics.[3,4] Personalized medicine plays a crucial role in addressing these challenges, and health professionals must adapt their current practices to account for changes in pharmacokinetics and pharmacodynamics associated with aging.[4,5] Additionally, they should be mindful of factors such as cognitive impairment, concurrent health issues, polypharmacy, orthostatic hypotension, falls, medication cost, side effects, visual and auditory limitations, social support, caregiver availability, and frailty.[4]

Hypertension is one of the most prevalent comorbid conditions in older people, rarely occurring in isolation.[6] It is a severe disease that significantly increases the risk of heart, brain, kidney, and other diseases. Approximately 1.4 billion people globally have high blood pressure.[7] Several studies, traditionally excluding older adults, especially those aged 80 years and above, have historically concentrated on guiding the screening and management of hypertension. Although the SPRINT trial demonstrated a systolic blood pressure (SBP) of less than 120 mm Hg, as compared with less than 140 mm Hg, resulted in lower rates of fatal and nonfatal major cardiovascular events and death from any cause in individuals aged greater than 50 year without diabetes and a previous stroke,[8] the treatment of elevated blood pressure in older people remains controversial.[4,9–11] The optimal SBP targets for older patients continue to be a subject of considerable debate, as various guidelines propose different thresholds ranging from strict (<120 mm Hg) to more lenient (SBP < 140 or < 150 mm Hg based on cardiovascular risk[11]; for additional discussion, refer to Supiano[12]).

Older patients are at a higher risk of adverse reactions to hypertension overtreatment, such as postural hypotension and falls.[9] Effective pharmacologic lowering of diastolic blood pressure can potentially diminish coronary perfusion and elevate the risk of myocardial infarction. However, concerns regarding the effect of low diastolic BP have been largely dismissed.[13] The use of alpha-blockers is linked to a higher risk of heart failure. Older individuals who persist in taking blood pressure medications despite experiencing hypotension face elevated risks of mortality and hospital admissions.[10] Moreover, the utilization of antihypertensive drugs is linked to adverse effects such as orthostatic hypotension, metabolic impacts, frailty, dizziness, syncope, falls, and, in certain studies, a potential deterioration in cognitive function among individuals with dementia.[14]

Mitigating harm associated with medication is especially challenging within the framework of multimorbidity and polypharmacy. However, judicious management of multiple medications may be warranted and advantageous in addressing intricate comorbidities in older patients, mainly when each drug is thoughtfully evaluated in the context of the patient's overall health and prognosis.[15] Polypharmacy is the concurrent use of multiple medications and is often defined as the routine use of 5 or more drugs. This includes over-the-counter prescription and traditional and complementary medicines a patient uses. The objective should be to minimize unwarranted polypharmacy, characterized by the imprudent prescription of an excessive number of medications, and promote justified polypharmacy. This involves the rational prescription of multiple drugs founded on the best available evidence while considering individual patient factors and the specific context of their health.[16]

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The global prevalence of polypharmacy is on the rise, particularly among older adults, and mainly encompasses prescription drugs. The number of daily medications tends to be generally proportional to the concurrent presence of chronic medical conditions.[15] Deprescribing is the process of withdrawal of an inappropriate medication, supervised by a health care professional to manage polypharmacy and improve outcomes.[17] Knowledge of potential adverse effects and consideration of patient factors across physical, social, and psychological domains is essential for deprescribing.[18]

WHO CAN BENEFIT FROM ANTIHYPERTENSIVE DEPRESCRIBING?

One component of good prescribing is deprescribing[19,20]; however, clinical guidelines frequently focus on how and when an antihypertensive medication should be initiated. There is often no information about when and how such drugs should be deprescribed, with clinical trials foregoing the opportunity to collect data on the effects of stopping antihypertensive medication during or at the end of the study period.[11] A strategy of deprescribing proves valuable when the ongoing antihypertensive regimen no longer corresponds to the care objectives, especially in scenarios like end-of-life care, where the potential for additional cardiovascular disease (CVD) or other prevention benefits is negligible. In these instances, deprescribing may be considered an acknowledgment of therapeutic futility. Also, antihypertensive medications might become unsuitable for individuals at a heightened risk of adverse events (**Table 1**).[21,22]

An essential aspect of deprescribing involves identifying medications that may be inappropriate for withdrawal in high-risk patients, aiming to prevent potential adverse events. However, this task is complex, as determining who is at high risk poses challenges. Moreover, this approach is not without risks itself, as discontinuing an antihypertensive medication to prevent a fall might inadvertently increase the likelihood of a more severe cardiovascular event, such as a stroke.[22] In response to this challenge, tools and guidelines have been developed to assist clinicians in evaluating the appropriateness of medications, facilitating the deprescribing of potentially inappropriate medications (PIMs), and recommending suitable alternatives, particularly for vulnerable populations.[23,24] These resources can support the entire deprescribing process or focus on specific aspects.[24] They may take an explicit approach, offering predefined criteria or lists of medications, or an implicit approach, relying on clinical judgment and expert opinion.

Some tools combine explicit and implicit methods to assess the appropriateness of medications.[23,24] Considering cultural, societal, and medical diversity, various tools and guidelines have been created to accommodate multiple health care settings. These resources aim to empower clinicians, aiding them in decision-making and enhancing their self-efficacy in medication management to improve care for vulnerable groups.[23] The 2 main sources of information about PIMs for older adults are the American Geriatrics Society Beers Criteria and STOPP/START.[25,26]

Older individuals are notably susceptible to the white coat effect, a clinical phenomenon wherein the systolic and diastolic blood pressure measured in a clinical setting is higher than the readings obtained through home blood pressure monitoring.[9,27] This transient change in blood pressure substantially impacts signs and symptoms and may lead to overtreatment, leading to errors in decision-making, thereby complicating treatment.[9] Almost 20% of hypertensive patients may have a white coat effect detected through blood pressure measurement at home, compared to the office measurement. The mean difference in blood pressure between the places can reach 10.1 mm Hg for systolic and 4.3 mm Hg for diastolic.[27] Relying solely on a single office blood pressure measurement may result in unnecessary treatment with antihypertensive drugs,

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Table 1
Discontinuing antihypertensive medication criteria and rationale for deprescribing in older people

Discontinuing Antihypertensive Medication Criteria	Rationale
White coat effect	For patients whose office blood pressure is above target when taking medication, it is suggested to check blood pressure at home.[30] If blood pressure is at goal on home blood pressure monitoring, or the patient has symptoms of hypotension, deprescribing antihypertensive medication should be considered.[9]
Orthostatic hypotension	Asymptomatic orthostatic hypotension is prevalent in older people. Excessive prescribing of antihypertensive medications targeting seated systolic blood pressure readings may occur in more than one-fourth of geriatric patients.[29]
Potentially inappropriate prescription	Potentially inappropriate medications, which have low evidence of effectiveness and a high risk of adverse events, should be deprescribed in older people, for example, central alpha-agonists and non-selective peripheral alpha-1 blockers for the treatment of hypertension.[26]
High-risk patients	Several older patients are at high risk of adverse reactions to antihypertensive treatment and this risk outweighs the benefits of treatment. In some cases, it may be inappropriate to deprescribe antihypertensive medications, especially if they have been prescribed for indications other than blood pressure management.[30] Deprescribing should occur when adverse drug events occur (eg, electrolyte disorders, falling from low blood pressure), when the regimen appears to be "overaggressive" (eg, blood pressure <110), or when blood pressure control is not consistent with goals of care (eg, end of life)
Prescribing cascades	Each antihypertensive class has predictable adverse effects that while, typically mild, may lead to predictable prescribing cascades. Drug-induced symptoms frequently go under reported and when reported are often misattributed as the manifestation of new disease.[29]

primarily due to the white coat effect. Home blood pressure monitoring is a safe and straightforward approach for identifying cases influenced by the white coat effect. This method allows for adjustments in dosage or medication, thereby mitigating unnecessary risks, particularly in the case of older patients.[9] (Additional information is provided in Burks C et al.[28])

Another essential clinical condition is orthostatic hypotension, which is prevalent in the older population[29] (between 30% and 50%)[11] and may be underdiagnosed. In an observational study, individuals aged 65 years or older, capable of standing, underwent screening for orthostatic hypotension. This condition was defined as a reduction in SBP of 20 mm Hg or greater or diastolic blood pressure of 10 mm Hg or greater after standing for 3 minutes. Clinic personnel measured sitting blood pressure after patients had been quietly seated in the examination room. Subsequently, patients stood for

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approximately 3 minutes, and blood pressure was recorded while standing. The prevalence of orthostatic hypotension was 18%. Physicians were more inclined to discontinue antihypertensive medication in patients who screened positive for orthostatic hypotension compared to those who did not.[29]

High-risk patients are individuals whose characteristics and medical history predispose them to an elevated risk of adverse events associated with antihypertensive therapy. These risk factors encompass advancing age, dementia, chronic kidney disease, prior adverse drug reactions, blood pressure maintained below 110 to 120 mm Hg (indicating overaggressive antihypertensive treatment), polypharmacy, and frailty. Adverse drug reactions may manifest as hypotension, syncope, falls, fractures, acute kidney injury, and electrolyte abnormalities. Certain antihypertensive classes may contribute to specific adverse reactions, such as acute kidney injury and electrolyte imbalances, while others are more closely associated with lowering blood pressure (eg, hypotension and syncope). Numerous conditions and factors may contribute to an individual's heightened risk of experiencing adverse events.[30]

Another effective strategy within deprescribing initiatives involves identifying prevalent prescribing cascades, where a second (potentially preventable) medication is prescribed in response to an adverse effect or drug reaction induced by another medication. For instance, the initiation of calcium channel blockers, known for causing peripheral edema, may lead clinicians to prescribe diuretics to mitigate this adverse effect. Another example is the common practice of prescribing antihypertensives following the initiation of nonsteroidal anti-inflammatories. Additionally, numerous widely used medications, including corticosteroids, estrogens, testosterones, certain antidepressants, and common over-the-counter cold remedies and supplements, may contribute to elevated blood pressure levels.[31,32]

WHAT ARE THE BENEFITS OR HARMS?

The ECSTATIC study examined the effect of deprescribing cardiovascular medications in community-dwelling patients aged 40 to 70 years. In this cluster, randomized nonblinded parallel-group active-control noninferiority study, general practitioners and practitioner nurses were trained to follow deprescribing guidelines for gradual dose reduction and monitoring blood pressure and cholesterol levels. No intervention was planned for the usual care group. The findings indicated that attempting to discontinue preventive cardiovascular medication in general practice patients with a predicted low 10 year CVD risk was deemed safe in the short term compared to standard care, with only a minimal difference observed in the increase of predicted 10 year CVD risk. However, after 2 years, 65% of the 1067 participants stopped a statin or antihypertensive, and 27% could maintain this. Compared to the usual care group, SBP was 6 mm Hg higher for the intervention group, and diastolic blood pressure was 4 mm Hg higher. Cost and quality-adjusted life years did not differ between the groups.[33]

In 2020, a Cochrane Review evaluated 6 trials involving 1073 participants aged 50 years and older, focusing on deprescribing antihypertensive medications for indications such as hypertension and/or primary prevention of CVD. The duration and follow-up of these trials varied from 3 to 12 months, and this short term was a limitation of these studies. The analysis revealed no significant impact on the primary endpoints of all-cause mortality (odds ratio [OR] 2.08, 95% confidence interval [CI] 0.79–5.46) or myocardial infarction (OR 1.86, 95% CI 0.19–17.98) when comparing the discontinuation and continuation of antihypertensives. Additionally, antihypertensive deprescribing did not show to increase the risk of adverse events.[34]

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The OPTIMISE trial investigated deprescribing of a single antihypertensive medication in participants aged 80 years or older, with a baseline SBP of less than 150 mm Hg (mean baseline 130 mm Hg) and already under treatment with 2 or more antihypertensives. Participants were randomized to a strategy of antihypertensive medication reduction (removal of 1 drug) or usual care, in which no medication changes were mandated. Primary care physicians participating in the study were provided with a medication reduction algorithm. They evaluated the medication regimens of each patient before the baseline. They determined which antihypertensive drug would be discontinued if the participant was assigned to the medication reduction group of the trial. Compared to the standard care group, most participants achieved the primary endpoint, maintaining an SBP less than 150 mm Hg at the 12 week follow-up (87.7% vs 86.4%, relative risk [RR] 0.98, 95% CI 0.92–1.05). Following the reduction in medication, the mean increase in SBP was 3.4 mm Hg (95% CI, 1.1–5.8 mm Hg). There were no significant differences in serious adverse effects. Two-thirds of the intervention group did not require any adjustments to their regimen after discontinuing the antihypertensive, indicating that successful withdrawal may be attainable for many patients.[35]

A limitation of these studies is the short duration in assessing the long-term impact and potential harm associated with antihypertensive medication withdrawal. The low harm observed during these trials does not definitively exclude the possibility of adverse events occurring over a more extended period. The delayed onset of complications, such as cardiovascular events, underscores the need for extended follow-up to comprehensively evaluate the safety profile of deprescribing interventions.

HOW TO DEPRESCRIBE ANTIHYPERTENSIVE DRUGS?

Although evidence supports the effectiveness and pharmacoeconomic benefits of deprescribing interventions, there is considerable heterogeneity in the types of interventions and the reporting of processes.[36]

Effective clinical practice should incorporate shared decision-making, wherein health care professionals discuss the risks and benefits of various treatment options with patients and their caregivers. However, it is recognized that implementing shared decision-making can pose challenges in the practical application of deprescribing.[37]

The initial step in determining the appropriateness of antihypertensive deprescribing involves obtaining accurate blood pressure measurements, particularly in older patients.[9] Accurately and consistently measuring blood pressure multiple times is essential for establishing a comprehensive profile of blood pressure peaks and troughs. This profile is crucial for making well-informed decisions regarding antihypertensives and setting blood pressure targets. In the older population, blood pressure readings demonstrate more significant variability than in the general population, and even slight variations in blood pressure measurement techniques can lead to significant effects. To ensure precision, blood pressure measurements should consider factors such as appropriate cuff size, simultaneous measurement on both arms (except in cases of unilateral subclavian artery stenosis), adjustments for underlying atrial fibrillation where cardiac stroke volume and blood pressure may vary beat by beat, and measurements taken in both lying and standing positions.[11] After measuring blood pressure in the sitting position, repeat the measurement in the standing position after 3 minutes and assess the possibility of orthostatic hypotension.[29] Home or ambulatory blood pressure measurements should be performed whenever possible.[9]

It is essential to conduct a thorough review of the medications taken by patients and engage in discussion with them regarding the outcomes and care goals. Patients should be informed about the evidence supporting the benefits of drugs that may

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be questionable. Collaborating with pharmacists and other health care professionals, engaging in discussions with patients and their caregivers, and utilizing clinical tools are valuable approaches that can assist physicians in optimizing medication lists and undertaking appropriate deprescribing when necessary.[38]

Tools such as STOPP/START[24] and the American Geriatrics Society Beers' criteria[26] can identify potentially inappropriate antihypertensive medications. Discontinuing antihypertensive medications may not be advisable, mainly if they were prescribed for reasons other than managing blood pressure. Antihypertensive medications should be tapered off sequentially, one at a time, with a 4 week interval between each withdrawal. When discontinuing beta-blockers, diuretics, or any other antihypertensive drugs prescribed at high doses, health care professionals should initially contemplate dose reduction before complete cessation. It is crucial to monitor the patient's SBP 4 weeks after discontinuing therapy to ensure it remains within the target range. In cases of uncontrolled blood pressure, health care professionals should contemplate reintroducing the previously discontinued medication at a lower dose (if feasible) or suggest alternative non-pharmacological strategies to effectively manage blood pressure.[22]

Additionally, it may be crucial to consider both blood pressure levels and cardiovascular risk, as continued treatment may remain suitable and beneficial for certain patients with multiple risk factors.[30] Agents with antihypertensive effects may benefit patients with other comorbidities and may be prescribed more specifically for these additional purposes.[11] Discontinuing beta-blockers for heart failure, atrial fibrillation, or ischemic heart disease, angiotensin converting-enzyme (ACE) inhibitors for heart failure or renal protection, and prazosin for prostatic symptoms could exacerbate the underlying medical conditions.[30]

CLINICS CARE POINTS

- Deprescribing antihypertensives in older adults should consider the active participation of patients and caregivers.
- Blood pressure measurements must be accurate: the effect of the white coat and orthostatic hypotension must be evaluated.
- A medication review considering the prescription of inappropriate antihypertensives and their gradual withdrawal should be carried out.
- Patients should be monitored continuously, and cardiovascular risk should be assessed.

DISCLOSURE

The authors have nothing to disclose.

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