Orthostatic Hypotension Screening in Older Adults Taking Antihypertensive Agents

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Orthostatic hypotension (OH), while not itself a disease, is an important physical finding in the setting of unexplained syncope or falls. All antihypertensive medications directly interfere with the normal cardiovascular responses (increased venous return, tachycardia, and vasoconstriction) to orthostatic stress. Regular screening for this condition in older adults with hypertension, as well as careful titration of antihypertensive medications, can greatly improve both mortality and quality of life in this vulnerable population.

Keywords: orthostatic hypotension, postural vitals, antihypertensives, syncope, geriatric medicine

Introduction

Orthostatic hypotension (OH) is an important physical finding in the setting of unexplained syncope or falls. Orthostatic hypotension is arbitrarily defined by the American Academy of Neurology as a reduction in the systolic blood pressure of at least 20 mm of Hg, or a reduction in the diastolic blood pressure of at least 10 mm of Hg within 3 minutes of standing.1 This condition becomes clinically significant when cerebral hypoperfusion occurs that results in lightheadedness, visual changes (dimming or blurring), leg weakness, headache, cognitive slowing, or loss of consciousness.2 Concomitant vascular disease may also result in more unusual presentations such as angina or transient ischemic attacks.3 Orthostatic hypotension has shown a direct negative association with the risk of myocardial infarction,4 stroke risk, and overall increased mortality.5

Asymptomatic OH has been shown in a large longitudinal study to have a prevalence of 16% in community-dwelling adults age 65 or more,6 rising to 68% in hospitalized older adults.7 Risk factors for OH include age,8 supine hypertension, autonomic dysfunction (due to diabetes or Shy-Drager syndrome),9 hypovolemia, or immobility.10 However, the most common iatrogenic cause of OH in older adults is due to the adverse effects of medications, especially antihypertensive agents.11

The Physiology of Orthostasis

In the supine position, a person's blood volume is distributed equally within the body. But after one minute of standing, approximately 500 mL of blood has moved to the vasculature in the legs. Thirty minutes of standing results in approximately 15% of plasma volume transferred to the interstitial tissue. This loss of fluid explains why some individuals experience orthostatically associated syncope after more prolonged periods of ambulation, as opposed to immediately upon standing.12

When assuming an upright posture, a person normally maintains blood pressure through a variety of mechanisms (Figure 1). Lower limb musculature contracts, resulting in an increase in venous return to the heart; the decrease in blood pressure with standing activates the arterial baroreflex13 and produces tachycardia and peripheral vasoconstriction; there is also activation of the renin-angiotensin-aldosterone axis, and increased production of other vasoactive agents such as endothelin and vasopressin. Many of these compensatory mechanisms are impaired by the pharmacodynamic effects of antihypertensive medications.14

Medications and Orthostatic Hypotension

A previous investigation of adult ambulatory veterans age 75 years and older has demonstrated that 55% of these patients have OH, with 33% experiencing symptoms.11 This study examined the relationship between the prescription of antihypertensives, alpha-blocking agents, diuretics, antidepressants, and antipsychotic agents and the presence of OH in the general population. The risk of OH was positively associated with the number of potentially OH-producing medications prescribed, with the prevalence of OH in patients receiving none, 1, 2, and greater than 3 of these agents being 35, 58, 60, and 65% respectively.11

Antihypertensive Medications and Orthostatic Hypotension

All antihypertensive medications directly interfere with normal cardiovascular response to orthostatic stress. One potential consequence of antihypertensive agents is impaired venous return. The normal increase in venous return due to lower limb muscular contraction is impaired by antihypertensives that result in hypovolemia. These primarily occur with diuretic agents such as hydrochlorothiazides.12 Tachycardic responses may also be compromised. The
Figure 1: Mechanisms of Blood Pressure Maintenance When in Upright Position

Pathophysiology of Orthostatic Hypotension

In the supine position, blood volume is distributed equally within the body.

After 1 minute of standing, approx. 500mL of blood has moved to vasculature of legs.

30 minutes of standing results in approx. 15% of plasma volume transferred to interstitial tissue.

The decrease in blood pressure with standing activates the arterial baroreflex and produces tachycardia and peripheral vasoconstriction.

Blood pressure rises

Salt retention

Aldosterone

Angiotensin II

ACE

Angiotensin I

Angiotensinogen

Renin

Blood pressure falls

Lower limb musculature contracts, resulting in an increase in venous return of blood to the heart.
normal tachycardic response to unloading of the carotid and aortic arterial baroreceptors with standing is impaired by beta-adrenergic receptor blockers (metoprolol and atenolol) as well as non-dihydropyridine calcium channel blockers such as verapamil or diltiazem.12

Finally antihypertensive medication can impair the vasoconstrictive response. Vasodilatory agents such as dihydropyridine calcium channel blockers (such as amlodipine, felodipine, and nifedipine), and direct vasodilators (such as hydralazine and minoxidil) impair the normal vasoconstrictive response to orthostatic stress. Vasocontriction is also impaired by agents that disable the renin-angiotensin-aldosterone axis such as angiotensin-converting enzyme inhibitors; centrally acting agents such as clonidine also impair the vasoconstrictive response.12

**Orthostatic Vitals—Technique**

Textbooks contain conflicting information as to how to measure orthostatic vitals, specifically how long to wait between supine and standing blood pressure measurements. Often teaching around this issue is quite anecdotal, with interpressure durations ranging between 0 and 3 minutes. A standardized investigation of this issue (using head-up tilt table testing) has shown that the average older adult with OH demonstrates a decrease in systolic blood pressure of at least 20 mm of Hg after an average of 85±20 seconds.15 One minute of head-up tilting has been shown to detect the majority (about 90%) of all individuals with OH, with all cases detectable within 3 minutes. Two minutes of upright tilting is necessary to detect a progressive pattern of OH (defined as a continuously progressive decrease in blood pressure on standing, which is much more likely to result in syncope).16 Therefore, a 1-minute orthostatic stress is likely sufficient for screening purposes (and should be done in all older adults on antihypertensive agents), but a longer duration (at least 2 minutes) of orthostatic stress is necessary to determine the severity and clinical significance of any OH detected on screening.16

**Orthostatic Vitals—Factors that Affect Reproducibility**

Orthostatic vitals have been shown to have poor overall reproducibility in older adults with symptomatic OH15 and in older adults with hypertension seen in a primary care setting.17 In fact, the repeatability coefficients, which are a marker of lower reproducibility, range from 54–65% in hypertensive older adults. This is much larger than the repeatability coefficients for baseline supine blood pressure in older adults with hypertension (31–44%).17 This indicates that multiple measures of orthostatic vitals are important in screening for OH, with at least two orthostatic drops detected to make a diagnosis.17

Is there any way to increase reproducibility of orthostatic vitals? Obviously it is important to always compare the same orthostatic stress (supine to standing) and use the same interpressure duration when comparing different orthostatic measures. In addition, orthostatic vitals have been shown to be less reproducible in OH patients with normal autonomic function since it is due to a fluctuating etiology such as hydration or medications. Therefore it is vital to document the time since the last antihypertensive was administered.15

Diurnal variations in blood pressure also greatly affect the reproducibility of orthostatic vitals. In normal subjects, blood pressure is lowest during the night, early in the morning and after meal consumption. Individuals with OH, however, demonstrate a nocturnal increase in blood pressure (due to their supine posture) as well as a much larger decrease in blood pressure upon arising in the morning. This reversal in the normal diurnal blood pressure variation explains why orthostatic vitals are much less reproducible when performed in the afternoon as compared to morning measurements.15

Successful screening for OH therefore requires multiple measures (at least two) to confidently detect this condition. As much as possible, measures should be performed the same time of day relative to meals and medication administration and will be most reproducible if done during morning hours.

**Orthostatic Hypotension and Antihypertensive Agents—Treatment**

Obviously, the easiest course of action to reduce symptomatic OH in older patients taking antihypertensives is to reduce the dosage or switch the type of medication.18 If hydration status is an issue, often improving oral fluid intake in combination with switching the antihypertensive to a nondiuretic agent can resolve the issue. Nonpharmacological therapies can also assist in helping with antihypertensive-related OH. These include reducing the speed of moving from a supine to standing position, and being aware of situations that will exacerbate OH such as alcohol consumption, eating large meals,19 hyperthermia, hot showers, straining at stool, and strenuous isometric exercise.2 Physical maneuvers such as squatting and leg crossing at the start of prodromal symptoms can also be quite effective at controlling symptoms, mainly due to the fact that they have been shown to increase blood pressure between 10 and 45 mm of Hg.20 Standard therapies for OH such as increased salt consumption, and use of mineralocorticoid agents (fludrocortisone) and alpha-1 agonists (midodrine) should be avoided in the setting of antihypertensive-induced OH since all of these therapies increase supine blood pressure.21

**Coexisting Supine Hypertension and OH**

How does one handle a patient that simultaneously has supine hypertension and orthostatic hypotension? This can be a difficult therapeutic situation since the patient is inadequately treated yet suffering from the adverse effects of antihypertensives. One other complicating factor is that supine hypertension has been shown to result in increased orthostatic hypotension, likely due to desensitization of the arterial baroreflex,15,22 although some have
disputed this relationship. Several issues to consider include, first, whether the orthostatic drop is clinically significant. Isolated OH has shown an inconsistent relationship with fall risk in community-dwelling older adults if asymptomatic. If the OH you have detected on screening is not accompanied by any falls, presyncope, or syncope, it does not likely have any clinical significance.

Second, consider whether the patient’s supine hypertension contributing to his/her OH. Hypertension itself can contribute to OH. Slowly titrating up the patient’s antihypertensive agent (no more often than once every 4 weeks and at the smallest possible dose change) can frequently result in normal supine blood pressure and improvement in OH due to resetting of the arterial baroreflex. This requires a large commitment of time and energy on the part of both physician and patient, due to the large number of follow-up visits for monitoring and medication adjustment.

Finally, it is worth evaluating whether the selected blood pressure targets are too rigorous. The recent HYVET (Hypertension in the Very Elderly Trial) demonstrated clinically significant improvements in stroke risk and mortality rate with much less rigorous blood pressure targets (target of 150/90 mm Hg, which only about half the subjects achieved). This suggests that much less rigorous targets among individuals older than 80 years of age can still have a large clinical impact. Although 150/90 makes for a reasonable initial target in older adults over 80 years of age for primary prevention, this target needs to be revised upwards based on the presence or absence of orthostatic intolerance. The best approach is to elevate your target blood pressure in 5 mm of Hg increments and see if the OH related-symptoms become more manageable. If your patient is unable to reach evidence-based blood pressure targets (such as 150/90) due to the presence of OH, then the patient’s blood pressure goals need to be individualized in order to maintain blood pressure as low as possible without causing symptoms.

**Conclusion**

Orthostatic hypotension is a common condition among older adults, especially those taking antihypertensive medications. Regular screening for this condition, as well as careful titration of antihypertensive medications, can greatly improve both mortality and quality of life in this vulnerable population.

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**Key Points**

- Asymptomatic OH has been shown in a large longitudinal study to have a prevalence of 16% in community-dwelling adults age 65 or more, rising to 68% in hospitalized older adults. Orthostatic hypotension has shown a direct negative association with the risk of myocardial infarction, stroke risk, and overall increased mortality.

- All antihypertensive medications directly interfere with the normal cardiovascular responses (increased venous return, tachycardia, and vasoconstriction) to orthostatic stress.

- Successful screening for OH requires multiple measures (at least two) to confidently detect this condition. As much as possible, measures should be the same time of day relative to meals and medication administration, and will be most reproducible if done during morning hours.

- The easiest course of action to reduce symptomatic OH in older patients on antihypertensives is to reduce the dosage or switch the type of medication. Non-pharmacological therapies can also assist in helping with antihypertensive related OH. Mineralocorticoid agents (fludrocortisone) and alpha-1 agonists (midodrine) should be avoided in the setting of antihypertensive induced OH since all of these therapies increase supine blood pressure.

- The recent HYVET (Hypertension in the Very Elderly Trial) demonstrated clinically significant improvements in stroke risk and mortality rate with much less rigorous blood pressure targets. This suggests that less rigorous targets in subjects older than 80 years of age can still have a large clinical impact.

**Clinical Pearls**

All older adults should be screened for OH at least twice per year. A patient has to be standing for at least one minute to screen for OH. Not all older patients can reach evidence-based blood pressure targets due to the presence of OH related symptoms. Therefore, each patient’s blood pressure goals need to be individualized in order to maintain blood pressure as low as possible without causing symptoms. A less ideal blood pressure target that can be maintained without adverse effects is preferable than merely abandoning control of a patient’s blood pressure because “they do not tolerate antihypertensives.”
Orthostatic Hypotension Screening

References