Orthostatic Hypotension (OH)

Presenter: Dr. Milta Little
Disclosure Statement: I have nothing to disclose.

Objectives: By the end of the session, participants will be able to...

• Define orthostatic hypotension (OH)
• List and describe the underlying causes of OH
• List first-line therapy for the treatment of OH
• List pharmacologic management for OH and potential adverse drug reactions

Expected Outcomes (Desired change in practice):

• Evaluate for postural blood pressure changes in nursing home residents with falls, cognitive decline, and other clinical risk factors
• Diagnose underlying causes of OH, which will drive treatment

Article for Review:


Additional Article:

• Palma JA and Kaufmann H. Management of orthostatic hypotension. Continuum (Minneap Minn) 2020; 26(1, autonomic disorders):154-177. This article is longer with more detail on the underlying causes and treatments, along with several useful figures.
Outline for Rapid Fire session

1. Case presentation: OH

A 73-year-old cis-gender man with moderate stage Alzheimer’s disease, benign prostatic hypertrophy, slow-transit constipation, erectile dysfunction, and stage 3a chronic kidney disease was seen for evaluation after an episode of brief unresponsiveness and collapse. The facility had hosted a traditional Thanksgiving dinner for residents and families. After the meal, he stood up, walked a few steps, and suddenly collapsed to the floor. He was unresponsive but came to in a few seconds, startled but not confused. His wife was with him and reported that he had no involuntary movements, loss of urine, or tongue biting. He was taken by ambulance to a local hospital per family request, where his blood pressure was 160/95 mm Hg. ECG, echocardiogram, complete blood cell count, metabolic panel, urinalysis, and a 24-hour Holter monitor were normal. He was diagnosed at that hospital stay with arterial hypertension, and antihypertensive treatment was recommended. On questioning during the current visit, he recalled having brief episodes of mild lightheadedness and blurry vision when standing up after meals, mostly after breakfast. His symptoms abate after sitting or lying down, and he had never lost consciousness until the episode that took him to the hospital. On physical examination, he appeared healthy. His cognition was at baseline and he had intact cranial nerves, normal deep tendon reflexes, flexor plantar responses, and no sensory deficits. His supine blood pressure was 157/102 mm Hg with a heart rate of 72 beats/min and after standing for 3 minutes was 119/75 mm Hg with a heart rate of 79 beats/min (change in heart rate [ΔHR]/change in systolic blood pressure [ΔSBP] ratio of 0.18 beats per minute/mm Hg). He had no orthostatic symptoms at the time. What do you do next?

2. Definition and pathophysiology of OH
   a. Drop of >20 mmHg in systolic blood pressure (BP) or >10 mmHg diastolic BP after standing for three minutes
   b. Impaired baroreflex – lack of sympathetic nervous system activation – no lower-limb/splanchnic vasoconstriction, lack of heart rate increase
   c. Symptoms: dizziness, lightheadedness, cognitive slowing, syncope, blurred/dimmed vision, upper body muscle pain, fatigue, dyspnea, and rarely angina

3. Underlying causes and work-up of OH
   a. Neurogenic – Parkinson Disease (PD), Lewy Body Disease (LBD), multiple systems atrophy (MSA), isolated autonomic failure/neuropathy (diabetes, amyloidosis)
   b. ~50% people with neurogenic OH also have neurogenic supine hypertension (nSH) – BP ≥140/90 after 5 min in supine position
   c. Post-prandial hypotension – drop of ≥10 mmHg SBP within 2 hours of eating
   d. Non-neurogenic – anemia, volume depletion, excessive venous pooling (varicose veins), medications, deconditioning, heart failure, adrenal insufficiency.
   e. Non-neurogenic causes of OH have normal baroreflexes with increased sympathetic activation and increased HR upon standing
   f. Commonly offending meds: SNRI, TCA, CCB, benzodiazepines, beta-blockers, diuretics, nitrates, dopaminergic agents
4. Non-pharmacologic management of OH
   a. Target and correct aggravating factors (meds, anemia, dehydration, etc)
   b. Avoid bed rest – seated/recumbent exercise, raise head of bed
   c. Avoid hot showers
   d. Volume expansion – avoid caffeine, alcohol; Increase fluid intake to 2-2.5 L per day with consideration of 500 mL bolus water drinking if able; liberalize salt intake
   e. Physical counter maneuvers: leg crossing, standing on tiptoes, stooping, squatting, and buttock clenching; avoid Valsalva
   f. Compression: abdominal binder or waist-high compression stockings, 15-20 mmHg
   g. Postprandial hypotension: small, frequent meals; avoid high-glycemic index carbs
   h. Concurrent nSH: elevate head and avoid bed during day, high glycemic index carb snack at bedtime

5. Pharmacologic management of OH
   a. Fludrocortisone – expands volume through sodium and water absorption (mineralocorticoid); 0.05-0.2 mg daily; increases risk of heart failure, kidney failure, hypokalemia, and worsens nSH
   b. Increase peripheral resistance
      i. Midodrine – alpha-1 adrenoreceptor agonist – vasoconstrictor; works well with abdominal binder; 2.5-15 mg BID to TID; avoid in BPH, urinary retention; avoid HS dosing
      ii. Droxdopa – norepinephrine precursor; 100-600 mg TID; consider for PD, MSA, LBD, amyloidosis; avoid HS dosing
   c. Pyridostigmine – acetylcholinesterase inhibitor – probably not very effective
   d. Erythropoietin in anemia of chronic disease
   e. Postprandial hypotension: acarbose (alpha-glucosidase inhibitor) 50-100 mg before meals or Octreotide – somatostatin analogue, inhibits GI vasodilator hormones, 0.2-0.4 mcg/kg subcut
   f. nSH – consider low-dose short-acting anti-HTN at night, e.g. nifedipine, clonidine, hydralazine, nebivolol, losartan
FIGURE 9-3
Flowchart of the management of neurogenic orthostatic hypotension. Removal of aggravating factors and initiation of nonpharmacologic measures must always precede the use of pharmacologic agents.

ΔHR = change in heart rate; ΔSBP = change in systolic blood pressure.

^ Supine.
Management of Orthostatic Hypotension

By Jose-Alberto Palma, MD, PhD; Horacio Kaufmann, MD, FAAN

ABSTRACT

PURPOSE OF REVIEW: This article reviews the management of orthostatic hypotension with emphasis on neurogenic orthostatic hypotension.

RECENT FINDINGS: Establishing whether the cause of orthostatic hypotension is a pathologic lesion in sympathetic neurons (ie, neurogenic orthostatic hypotension) or secondary to other medical causes (ie, non-neurogenic orthostatic hypotension) can be achieved by measuring blood pressure and heart rate at the bedside. Whereas fludrocortisone has been extensively used as first-line treatment in the past, it is associated with adverse events including renal and cardiac failure and increased risk of all-cause hospitalization. Distinguishing whether neurogenic orthostatic hypotension is caused by central or peripheral dysfunction has therapeutic implications. Patients with peripheral sympathetic denervation respond better to norepinephrine agonists/precursors such as droxidopa, whereas patients with central autonomic dysfunction respond better to norepinephrine reuptake inhibitors.

SUMMARY: Management of orthostatic hypotension is aimed at improving quality of life and reducing symptoms rather than at normalizing blood pressure. Nonpharmacologic measures are the key to success. Pharmacologic options include volume expansion with fludrocortisone and sympathetic enhancement with midodrine, droxidopa, and norepinephrine reuptake inhibitors. Neurogenic supine hypertension complicates management of orthostatic hypotension and is primarily ameliorated by avoiding the supine position and sleeping with the head of the bed elevated.

INTRODUCTION

Orthostatic hypotension is defined as a sustained reduction in systolic blood pressure of at least 20 mm Hg or a reduction in diastolic blood pressure of at least 10 mm Hg, usually within the first 3 minutes of standing or head-up tilt on a tilt table. Thus, a diagnosis of orthostatic hypotension requires blood pressure measurements. Orthostatic hypotension is not a symptom but a sign that usually indicates volume depletion, impaired peripheral vasoconstriction, or both. When orthostatic hypotension impairs perfusion to organs above the level of the heart, most notably the brain, it causes disabling symptoms that reduce quality of life and increase morbidity and mortality.
Orthostatic hypotension is frequent in the elderly due to a variety of medical conditions, such as intravascular volume depletion, blood pooling (ie, varicose veins\(^2\)), severe anemia, antihypertensive medications, and physical deconditioning; in these patients, orthostatic hypotension improves dramatically or resolves after the underlying cause is treated. In a minority of patients, orthostatic hypotension is due to reduced norepinephrine release from postganglionic sympathetic nerves, resulting in defective vasoconstriction when assuming the upright position.\(^3\) This is referred to as neurogenic orthostatic hypotension\(^3\) and is most frequently seen in patients with diabetes mellitus; neurodegenerative disorders caused by abnormal accumulation of α-synuclein (ie, synucleinopathies); and small fiber neuropathies caused by amyloid, autoimmune, or paraneoplastic diseases.\(^3,4\) Patients with high spinal cord lesions can experience neurogenic orthostatic hypotension when sitting or when placed in an upright position for rehabilitation due to lack of baroreflex-mediated activation of spinal sympathetic neurons.\(^5\) Complicating the management of neurogenic orthostatic hypotension is neurogenic supine hypertension, which occurs in approximately 50% of patients with neurogenic orthostatic hypotension.\(^6\)

**Epidemiology and Public Health Impact**

In the general population, the prevalence of orthostatic hypotension increases with age, and the numbers vary according to different clinical settings.\(^4,7,8\) In large epidemiologic studies, such as the Cardiovascular Health Study, the prevalence of orthostatic hypotension in patients older than 65 years of age was approximately 20%, although only 2% had symptoms.\(^9\) One factor influencing the high prevalence of orthostatic hypotension in the elderly is the frequency of use of antihypertensive medications.\(^10\) Vasodilators (eg, α-adrenergic blockers, calcium channel blockers, nitrates), opioids, tricyclic antidepressants, and alcohol are frequently associated with orthostatic hypotension. In elderly patients, orthostatic hypotension frequently causes or contributes to hospitalization, and it is present in 25% of patients presenting with syncope in the emergency department.\(^11\) The estimated orthostatic hypotension–related hospitalization rate is 36 per 100,000 adults and can be as high as 233 per 100,000 patients older than 75 years of age, with a median length of stay of 3 days and an overall in-hospital mortality rate of 0.9%.\(^7\) In inpatient series, the prevalence of orthostatic hypotension in elderly patients is as high as 60%.\(^12,13\) Orthostatic hypotension increases the risk of falls, cardiovascular disease, and all-cause mortality.\(^14–21\)

Neurogenic orthostatic hypotension affects approximately 20% of unselected patients with type 1 or type 2 diabetes mellitus, but it can be as high as 65% (ie, 23 million people in the United States) with increasing age and duration of diabetes mellitus.\(^22–24\) Neurogenic orthostatic hypotension is also common in patients with neurodegenerative synucleinopathies, disorders characterized by the abnormal accumulation of the misfolded protein α-synuclein in the central and peripheral nervous systems, such as Parkinson disease, dementia with Lewy bodies, pure autonomic failure, and multiple system atrophy. The prevalence of neurogenic orthostatic hypotension is 50% in Parkinson disease (ie, 500,000 people in the United States), 70% in multiple system atrophy, and 100% in pure autonomic failure. Other rare causes of neurogenic orthostatic hypotension include a number of genetic and autoimmune disorders. Neurogenic orthostatic hypotension is associated with increased morbidity, including poorer

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**KEY POINTS**

- Diagnosing orthostatic hypotension requires blood pressure measurements. The presence of orthostatic intolerance is not sufficient or necessary to diagnose orthostatic hypotension.
- Orthostatic hypotension is very common in the elderly, usually due to drug effects, volume depletion, or cardiovascular deconditioning.
- Neurogenic orthostatic hypotension is a feature of neurologic disorders affecting sympathetic pathways, including diabetes mellitus, neurodegenerative synucleinopathies, and amyloid neuropathies.
prognosis; development of cardiovascular, renal, and cerebrovascular disease; and cognitive impairment.

Neurogenic orthostatic hypotension occurs in up to 80% of patients with spinal cord injury resulting in quadriplegia and 50% of those with paraplegia immediately after the injury. Position changes during physical therapy induce orthostatic hypotension in 74% of patients with high spinal cord injury, which is symptomatic in 59%.

CLINICAL FEATURES AND DIFFERENTIAL DIAGNOSIS
Orthostatic hypotension can be symptomatic or asymptomatic. Symptoms are a consequence of hypoperfusion of the brain (causing dizziness, lightheadedness, cognitive slowing, [FIGURE 9-1] and syncope), the retina and visual pathways (causing blurry, dimmed vision), the upper body muscles (causing “coat hanger” pain), the lungs (causing fatigue and dyspnea due to hypoperfusion of the

![Blood pressure and cerebral blood flow in a patient with neurogenic orthostatic hypotension.](image)

**FIGURE 9-1**
Blood pressure and cerebral blood flow in a patient with neurogenic orthostatic hypotension. The upper tracing shows blood flow velocity as measured by middle cerebral artery (MCA) transcranial Doppler ultrasound, which indicates cerebral blood flow. The lower tracing shows continuous blood pressure acquired with plethysmography. When the patient is in the supine position, both blood pressure (121/84 mm Hg) and mean velocity (Vm) of MCA blood flow (54 cm/s) are normal. When the patient stands up, blood pressure plummets rapidly to 66/54 mm Hg and cerebral blood flow falls by nearly 50% (Vm, 29 cm/s). The patient becomes symptomatic, feels lightheaded and about to faint, and is unable to remain standing. Patient sits down and his blood pressure increases to 93/62 mm Hg. Although this blood pressure is still low, the patient is not symptomatic anymore because the Vm increased to 44 cm/s, indicating almost normal cerebral blood flow. The blood pressure of a patient with symptomatic orthostatic hypotension does not have to return to normal values for the patient to become asymptomatic but only to increase above the lower limit of cerebral autoregulation.

Vm = mean velocity.
apices), and, rarely, the heart (causing angina even with patent coronary arteries). Symptoms appear exclusively upon standing up and abate when sitting and lying down. Severely afflicted patients are unable to leave the supine position without experiencing presyncopal symptoms or losing consciousness.

In patients with neurogenic orthostatic hypotension, symptoms worsen during exercise and after meals (postprandial hypotension). Marked worsening occurs after prolonged bed rest that results in striatal and myocardial muscle atrophy. These muscle changes of physical deconditioning impair both the skeletal “muscle pump” that helps venous return to the heart during active movements and left ventricular contraction reducing cardiac output. Symptoms are worse in the morning because of overnight pressure natriuresis causing intravascular volume depletion in the morning.

In patients with neurogenic orthostatic hypotension, it is imperative to perform a careful neurologic examination with particular attention to subtle signs of parkinsonism or cerebellar ataxia as well as cognitive impairment or dream-enactment behavior indicative of probable rapid eye movement (REM) sleep behavior disorder. Any of these neurologic findings suggest that, in addition to autonomic failure, the patient has central nervous system (CNS) abnormalities and that autonomic failure is likely the presenting feature of a more widespread CNS synucleinopathy: Parkinson disease, dementia with Lewy bodies, or multiple system atrophy. Patients with chronic autonomic failure without motor, cognitive, or sensory symptoms receive a diagnosis of pure autonomic failure; this may remain as a restricted autonomic syndrome or patients may develop a CNS synucleinopathy years later. In rare cases, patients with isolated autonomic failure have a chronic form of an autoimmune autonomic neuropathy. If sensory symptoms accompany neurogenic orthostatic hypotension, a small fiber neuropathy should be suspected. Most commonly, as in diabetes mellitus or amyloidosis, sensory symptoms are length dependent (affecting the distal areas of extremities) and can include burning pain or absent/reduced pain and temperature sensation. Less commonly, as in paraneoplastic and immune-mediated neuropathies or ganglionopathies, sensory symptoms can be patchy and diffuse, sometimes severe and widespread, resulting in devastating sensory proprioceptive ataxia. A family history of neurogenic orthostatic hypotension and sensory symptoms suggests hereditary transthyretin amyloidosis.

In patients presenting with “orthostatic intolerance” (ie, difficulty maintaining the upright position), it is necessary to determine whether symptoms are due to orthostatic hypotension or to other causes. In patients reporting typical symptoms but without a fall in blood pressure within 3 minutes of standing, a more prolonged orthostatic stress with a tilt-table test may be necessary to define the condition. Patients with milder or earlier forms of autonomic failure may experience orthostatic hypotension after a longer time of standing (ie, delayed orthostatic hypotension). In patients with vasovagal syncope, prolonged tilt may reproduce an episode. Not infrequently, patients may present with symptoms mimicking those of orthostatic hypotension but without an identified fall in blood pressure, including patients with vestibular disorders, gait abnormalities, CNS depression from alcohol and drug use, and “the inebriationlike syndrome” (in which patients with parkinsonism report feeling imbalanced and unsteady, as if they were slightly inebriated, but unrelated to alcohol intake). Conversely, patients with cognitive impairment may not accurately identify symptoms of organ hypoperfusion, despite low blood pressure when standing.
If sustained orthostatic hypotension is confirmed, it is key to establish whether the cause is a pathologic lesion in sympathetic neurons (ie, neurogenic orthostatic hypotension) or if it is secondary to other medical causes (ie, non-neurogenic orthostatic hypotension), such as anemia- or dehydration-related volume depletion, excessive venous pooling sometimes aggravated by varicose veins, or medication side effects (eg, from alpha-blockers for benign prostate hyperplasia, antihypertensive agents, diuretics, tricyclic antidepressants, opioids, benzodiazepines, and antiparkinsonian agents).

**TABLE 9-1** lists features that are useful to distinguish neurogenic versus non-neurogenic orthostatic hypotension. A heart rate increase of at least 0.5 beats/min for each mm Hg fall in systolic blood pressure (ie, change in heart rate $\DeltaHR$ / change in systolic blood pressure $\DeltaSBP$ ratio of $\geq 0.5$ beats per minute/mm Hg) has very high sensitivity and specificity to diagnose non-neurogenic orthostatic hypotension.

![TABLE 9-1](image-url)
hypotension (CASE 9-1). Conversely, a $\Delta HR/\Delta SBP$ ratio of <0.5 beats per minute/mm Hg strongly suggests neurogenic orthostatic hypotension.43

**GENERAL PRINCIPLES OF MANAGEMENT**

Because normalizing blood pressure is not possible, the goal of treatment in patients with orthostatic hypotension is to attenuate symptom burden and reduce target organ damage and mortality. Expert consensus guidelines for the treatment of neurogenic orthostatic hypotension are available.44 Approximately 50% of patients with neurogenic orthostatic hypotension also have neurogenic supine hypertension (a systolic blood pressure of at least 140 mm Hg or a diastolic blood pressure of at least 90 mm Hg after at least 5 minutes in the supine resting position), which poses a therapeutic challenge as treating one exacerbates the other.6 The steps of management include correcting aggravating factors and initiating nonpharmacologic measures before using pharmacologic therapies (FIGURE 9-3).44

Patients with asymptomatic neurogenic orthostatic hypotension usually require education and nonpharmacologic measures only. An exception to this might be patients with cognitive impairment who might not recognize symptoms of neurogenic orthostatic hypotension.42 Patients with hypotension-related symptoms of brain hypoperfusion do require treatment to increase standing blood pressure above the lower limit of cerebral autoregulation, ideally without aggravating neurogenic supine hypertension.45,46 The degree of tolerable hypertension when supine is unknown.

**Correction of Aggravating Factors**

Correction of aggravating factors can increase blood pressure sufficiently to improve orthostatic tolerance in some patients and should be the first step in the management of neurogenic orthostatic hypotension.

**DRUGS.** Medications that reduce intravascular volume or trigger vasodilatation can cause or worsen orthostatic hypotension. These drugs include nitrates, tricyclic antidepressants, diuretics, calcium channel blockers, alpha-blockers (usually prescribed for benign prostatic hypertrophy), phosphodiesterase-5 inhibitors (eg, sildenafil for erectile dysfunction), centrally acting $\alpha_2$-agonists (eg, clonidine or tizanidine), and beta-blockers, as illustrated in CASE 9-1. Levodopa and dopamine agonists may also lower blood pressure, and a dose adjustment may be considered based on an individual risk-benefit assessment.10,16,18,47

**ANEMIA.** Anemia of chronic disease is common in patients with neurogenic orthostatic hypotension.48 Anemia reduces blood viscosity and oxygen-carrying capacity and, consequently, worsens orthostatic hypotension. Hemoglobin scavenges nitric oxide, which is a potent vasodilator19; it is therefore possible that nitric oxide–mediated mechanisms enhance vasodilation in patients with orthostatic hypotension and anemia.30 Therefore, anemia must be investigated and treated appropriately. Increasing the red cell mass with recombinant erythropoietin improves orthostatic hypotension.31

**Nonpharmacologic Management**

Patient education on nonpharmacologic measures is the cornerstone of successful management of orthostatic hypotension. Nonpharmacologic treatments for orthostatic hypotension are listed in TABLE 9-2.52–54

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**KEY POINTS**

- A heart rate increase of at least 0.5 beats/min for each 1 mm Hg fall in systolic blood pressure ($\Delta HR/\Delta SBP$ ratio $\geq 0.5$ beats per minute/mm Hg) is sensitive and specific to diagnose non-neurogenic orthostatic hypotension.

- Treatment of orthostatic hypotension should be geared to the patients’ symptoms and their impact on daily function rather than a target blood pressure.

- The initial treatment of orthostatic hypotension focuses on nonpharmacologic measures first: removing offending medications, increasing salt and fluid intake, using compression garments, and instituting physical maneuvers and exercise.

- Drugs that reduce intravascular volume (eg, diuretics) or induce vasodilatation (eg, $\alpha$-adrenergic blockers, nitrates, phosphodiesterase-5 inhibitors, tricyclic antidepressants, centrally acting $\alpha$-adrenergic agonists) exacerbate orthostatic hypotension and worsen symptoms; thus, they should be reduced or discontinued.

- In patients with orthostatic hypotension, anemia should be investigated and treated.
A 72-year-old man presented with a 6-month history of orthostatic lightheadedness, which he first noticed after mild exercise. Lightheadedness was often accompanied by blurry vision and a dull pain in both shoulders and the back of his neck, shortness of breath, and, rarely, chest discomfort. He was taking furosemide 40 mg/d for “swollen legs,” amitriptyline 200 mg/d for depression, diazepam 5 mg 3 times a day for anxiety, and tamsulosin 0.8 mg in the morning for benign prostatic hyperplasia.

His neurologic examination was normal. His blood pressure in the supine position was 139/91 mm Hg with a heart rate of 89 beats/min. After 3 minutes standing, his blood pressure fell to 79/48 mm Hg with a heart rate of 123 beats/min, and he was severely lightheaded (change in heart rate [$\Delta HR$]/change in systolic blood pressure [$\Delta SBP$] ratio of 0.56 beats per minute/mm Hg) (FIGURE 9-2).

His ECG, complete blood cell count, and metabolic panel were normal. His plasma norepinephrine level when supine was normal at 198 pg/mL and increased to 491 pg/mL after 3 minutes of standing. The patient was instructed to discontinue furosemide and tamsulosin and switch amitriptyline to fluoxetine 20 mg/d.

At 4-week follow-up, his blood pressure in the supine position was 142/87 mm Hg with a heart rate of 81 beats/min. After 3 minutes of standing, his blood pressure was 131/79 mm Hg with a heart rate of 92 beats/min. He was asymptomatic.

This is a case of non-neurogenic orthostatic hypotension, a problem frequently caused by drugs with well-known hypotensive side effects, including the diuretic furosemide, the $\alpha$-adrenergic blocker tamsulosin, and the tricyclic antidepressant amitriptyline. General physical and neurologic examination are normal, with the exception of severe orthostatic hypotension with a significant increase in heart rate, with a change in heart rate ($\Delta HR$)/change in systolic blood pressure ($\Delta SBP$) ratio above 0.5 beats per minute/mm Hg, indicative of non-neurogenic orthostatic hypotension.

FIGURE 9-2  
Blood pressure and heart rate of the patient in CASE 9-1 supine and standing. The tracing shows severe orthostatic hypotension with a significant compensatory increase in heart rate, with a change in heart rate ($\Delta HR$)/change in systolic blood pressure ($\Delta SBP$) ratio above 0.5 beats per minute/mm Hg, indicative of non-neurogenic orthostatic hypotension.
LIFESTYLE, PHYSICAL ACTIVITY, AND MEALS. Hot, humid weather and environments cause vasodilatation and exacerbate orthostatic intolerance. Consequently, hot showers and saunas should be avoided. Short periods of bed rest worsen neurogenic orthostatic hypotension by causing cardiovascular deconditioning. The symptomatic burden can result in reluctance to stand up and avoidance of physical activity; physical immobility and skeletal muscle loss, in turn, worsen the severity of orthostatic hypotension. This results in a vicious cycle of deconditioning. It is therefore important for patients not to stop exercising, but to exercise in a recumbent or seated position (eg, using a stationary bicycle or a rowing machine) as those positions are better tolerated than the standing position. Exercise in a swimming pool is recommended, as the hydrostatic pressure of water counteracts the gravity-induced fall in blood pressure and improves orthostatic tolerance. Of note, patients must be very careful when getting out of the swimming pool, as the sudden decrease of hydrostatic pressure when exiting the pool can trigger venous pooling and worsen symptoms of orthostatic hypotension.

Food digestion is associated with blood pooling within the gastrointestinal (splanchnic) circulation. Normally, this is compensated for by increases in sympathetic nerve traffic causing splanchnic vasoconstriction. In patients with
neurogenic orthostatic hypotension, however, vasoconstriction is deficient, and some patients become hypotensive within 2 hours of eating.\(^1,57\) This is referred to as postprandial hypotension, and it is particularly pronounced after high glycemic index carbohydrate-rich meals. Low glycemic index carbohydrates are preferable, and frequent smaller meals should be implemented. Alcohol should be avoided during the daytime as it is a vasodilator. Alternatively, a high-carbohydrate treat or a glass of alcohol can be reserved for before bedtime, as these could contribute to managing supine hypertension.

**VOLUME EXPANSION.** Less intravascular volume causes reduced circulating blood volume and aggravates the blood pressure drop when standing. This is particularly relevant in elderly patients who are chronically volume depleted.\(^58\) It is important that patients and families understand the diuretic effects of caffeine and alcohol, a potent vasodilator. Patients should avoid sugary beverages (eg, sodas, bottled juices) as high glycemic index carbohydrates can induce or worsen hypotension.\(^59\) Water and salt liberalization are necessary to expand intravascular volume. Ideally, daily fluid intake should be 2 L to 2.5 L of water. In patients with neurogenic orthostatic hypotension, bolus water drinking (500 mL [16 oz]) produces a marked increase in blood pressure.\(^60,61\) Bolus water drinking has a fast pressor effect (the blood pressure increases within 5 to 10 minutes), which can be useful as a rescue measure, although the effect is relatively short (30 to 45 minutes). Patients should increase salt intake by adding 1 teaspoon of salt to a healthy diet. Some patients prefer using salt tablets (0.5 g to 1.0 g), although they may cause abdominal discomfort.

**PHYSICAL COUNTERMANEUVERS.** A number of physical countermaneuvers can help maintain blood pressure and reduce orthostatic symptoms during daily activities, including leg crossing, standing on tiptoes, stooping, squatting, and buttock clenching.\(^52\) Making sure that patients understand the effect of gravitational fluid shifts on blood pressure and orthostatic symptoms is key. Patients should be instructed to change positions gradually and briefly sit before standing. Straining with a closed glottis and other Valsalva-like maneuvers cause a sudden and severe fall in blood pressure and should be avoided.

**TABLE 9-2 Nonpharmacologic Treatments for Orthostatic Hypotension**

- Liberalization of salt consumption
- Liberalization of water intake (up to 2.5 L/d)
- Acute water bolus (drinking 500 mL water)
- Sleeping with the head of the bed raised 30 to 45 degrees with the help of an electric bed or mattress
- Physical activity with recumbent exercises (eg, stationary bicycle, rowing machine) or in a swimming pool
- Physical countermaneuvers (eg, standing up slowly, leg crossing, buttock clenching)\(^52\)
- Abdominal binder\(^53\)
- Waist-high compression stockings producing at least 15 mm Hg to 20 mm Hg pressure\(^54\) (knee-high or thigh-high stockings are typically not useful)
COMPRESSION GARMENTS. Elastic compression stockings apply counterpressure to the lower limbs and abdomen, reducing venous pooling. High-waist stockings producing at least 15 mm Hg to 20 mm Hg compression are effective to increase venous return and increase blood pressure. However, a major problem with the use of compression stockings is noncompliance. Elderly patients, patients with movement disorders, and those with sensory neuropathy may struggle to put the stockings on, which limits their applicability in everyday life. Elastic abdominal binders can be a good alternative. A recently developed abdominal binder that inflates automatically only on standing and provides sustained splanchnic venous compression (40 mm Hg) showed promising results in patients with neurogenic orthostatic hypotension.

SLEEPING WITH THE HEAD OF THE BED RAISED. Neurogenic supine hypertension is frequent in patients with neurogenic orthostatic hypotension. It is a side effect of antihypotensive treatment, but it also occurs in untreated patients. Managing neurogenic supine hypertension in patients with neurogenic orthostatic hypotension can be challenging, as treating one usually exacerbates the other. During the daytime, the best treatment is to avoid the supine position. Patients can sit in a reclining chair with their feet on the floor if they need to nap or rest. At night, elevating the head of the bed at least 30 to 45 degrees (accomplished with an electric bed or mattress) is effective to lower the blood pressure. Avoiding nocturnal supine hypertension with postural changes reduces the exaggerated nocturnal diuresis and natriuresis characteristic of these patients, therefore reducing the overnight fluid loss and ameliorating orthostatic hypotension in the morning. The use of pressor agents should be avoided within at least 4 hours before bedtime. Eating high glycemic index carbohydrate snacks or drinking a glass of wine right before going to bed contributes to hypotension and can therefore be harnessed to decrease nocturnal supine hypertension.

Pharmacologic Management
Despite removal of aggravating factors and implementing nonpharmacologic methods, many patients remain symptomatic and require pharmacologic treatment. Current pharmacologic approaches are based on two complementary strategies: (1) expanding intravascular volume with fludrocortisone and (2) increasing peripheral vascular resistance with midodrine, droxidopa, or norepinephrine reuptake inhibitors. Selection of one strategy or the other or both strategies depends on the specific features and needs of each patient as well as the degree of peripheral sympathetic denervation. Pharmacologic strategies can be combined (TABLE 9-3). When medications for neurogenic orthostatic hypotension are implemented, patients should be taught to avoid the horizontal position, sleep with the head of the bed raised 30 to 45 degrees, and measure their own blood pressure. They should provide a series of blood pressure recordings taken over several days to their clinician, including blood pressure taken when supine, sitting, and standing upon awakening; before and 1 hour after lunch; and before retiring to bed. Alternatively, ambulatory blood pressure monitors can be employed. Ambulatory monitors also measure blood pressure during sleep and can define the circadian blood pressure patterns before and after pharmacologic treatment.

LOCALIZING THE LESION. When planning therapeutic strategies in patients with neurogenic orthostatic hypotension, localization of the autonomic

KEY POINTS
- Because carbohydrate-rich meals trigger insulin, a potent vasodilator, patients with neurogenic orthostatic hypotension should reduce carbohydrate content, eat smaller and more frequent meals, and choose low glycemic index carbohydrates.
- Bolus water drinking produces a marked, albeit short-lived, increase in blood pressure in patients with neurogenic orthostatic hypotension.
- Waist-high compression stockings are effective to increase blood pressure in patients with neurogenic orthostatic hypotension, although compliance is very low. Elastic abdominal binders are a good alternative.
- Sleeping with the head of the bed raised 30 to 45 degrees reduces nocturnal hypertension, thus decreasing natriuresis, which, in turn, prevents volume depletion overnight and improves orthostatic tolerance the next morning.
- When medications for neurogenic orthostatic hypotension are used, patients should be taught to avoid the flat position, sleep with the head of the bed raised 30 to 45 degrees, and measure their own blood pressure.
lesion is important and has therapeutic implications (TABLE 9-4). Peripheral sympathetic neurons are affected in Lewy body disorders (Parkinson disease, dementia with Lewy bodies, pure autonomic failure) as well as in amyloidosis and autoimmune autonomic neuropathies but typically are spared in multiple system atrophy. More accurate than the clinical diagnosis is to determine the degree of sympathetic denervation by measuring plasma norepinephrine levels. Because norepinephrine is released by postganglionic sympathetic neurons, low levels of plasma norepinephrine in a patient with neurogenic orthostatic hypotension indicates sympathetic denervation (ie, a peripheral lesion), whereas normal or elevated norepinephrine levels indicate decentralization (ie, a central lesion), although considerable overlap exists. Determination of norepinephrine levels should be made in patients who are not taking norepinephrine precursor or reuptake inhibitors.

**VOLUME EXPANSION.** Two strategies can be used to expand intravascular volume in patients with orthostatic hypotension: fludrocortisone and erythropoietin.

**FLUDROCORTISONE.** Fludrocortisone is a synthetic mineralocorticoid that increases renal sodium and water reabsorption, therefore expanding intravascular volume and increasing blood pressure in all positions. It also enhances the pressor effect of adrenergic agonists. Fludrocortisone is perhaps the most frequently prescribed agent for the treatment of orthostatic hypotension.

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### TABLE 9-3 Mainstream Pharmacologic Treatments for Neurogenic Orthostatic Hypotension

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Recommended Dosage</th>
<th>Mechanism of Action</th>
<th>Side Effects</th>
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<tbody>
<tr>
<td><strong>Specifically approved for orthostatic hypotension</strong></td>
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<tr>
<td>Midodrine</td>
<td>2.5–15 mg 2 or 3 times a day (dosed morning, midday, and 3–4 hours before bedtime) or tailored to the patient’s needs</td>
<td>Direct α₁-adrenergic receptor agonist</td>
<td>Supine hypertension, piloerection (“goose bumps”), scalp itching, urinary retention; caution in congestive heart failure and chronic renal failure</td>
</tr>
<tr>
<td>Droxidopa</td>
<td>100–600 mg 3 times a day (dosed morning, midday, and 3–4 hours before bedtime) or tailored to the patient’s needs</td>
<td>Synthetic norepinephrine precursor</td>
<td>Supine hypertension, headache, nausea, fatigue; caution in congestive heart failure and chronic renal failure</td>
</tr>
<tr>
<td><strong>Not specifically approved for orthostatic hypotension</strong></td>
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<tr>
<td>Atomoxetine</td>
<td>10–18 mg 2 times a day</td>
<td>Norepinephrine reuptake inhibitor</td>
<td>Supine hypertension, insomnia, irritability, decreased appetite</td>
</tr>
<tr>
<td>Fludrocortisone</td>
<td>0.05–0.2 mg once a day; no benefit with dosages higher than 0.2 mg/d</td>
<td>Synthetic mineralocorticoid, volume expander that increases sodium and water reabsorption</td>
<td>Supine hypertension, hypokalemia, renal failure, edema, target organ damage; caution in congestive heart failure</td>
</tr>
<tr>
<td>Pyridostigmine</td>
<td>30–60 mg 2 or 3 times a day</td>
<td>Acetylcholinesterase inhibitor</td>
<td>Abdominal cramps, diarrhea, sialorrhea, excessive sweating, urinary incontinence</td>
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</tbody>
</table>
despite the fact that it is not approved by the US Food and Drug Administration (FDA) for this indication. Because activation of renal mineralocorticoid receptors results in inflammation and fibrosis and may have a direct nephrotoxic effect leading to a faster decline in renal function and hypertension, fludrocortisone should be used with extreme caution in the treatment of orthostatic hypotension, preferably for short-term periods, and the dosage should never be higher than 0.2 mg/d. Higher dosages do not improve therapeutic effects but intensify side effects. Fludrocortisone usually requires at least 7 days of treatment to exert significant clinical effect. Short-term side effects are frequent and include supine hypertension, hypokalemia, and ankle edema. Patients receiving fludrocortisone must eat potassium-rich foods or take potassium supplements (potassium chloride 20 mEq/d) to reduce the risk of hypokalemia. Long-term use exacerbates hypertension and organ damage, including left ventricular hypertrophy and renal failure, and is associated with a higher risk of all-cause hospitalization in patients with orthostatic hypotension.

ERYTHROPOIETIN. It is important to test for and treat anemia as it is common in patients with cardiovascular autonomic failure and frequently contributes to hypotension. If anemia is deemed to be idiopathic (ie, anemia of chronic disease), treatment with erythropoietin should be considered. Erythropoietin increases standing blood pressure and improves orthostatic tolerance in patients with orthostatic hypotension. Recombinant human erythropoietin is administered subcutaneously at doses between 25 U/kg and 75 U/kg 3 times a week until the

<table>
<thead>
<tr>
<th>TABLE 9-4 Distinguishing Features of Peripheral and Central Autonomic Lesions Causing Neurogenic Orthostatic Hypotension</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Peripheral Autonomic Lesion</strong></td>
</tr>
<tr>
<td>Plasma norepinephrine levels</td>
</tr>
<tr>
<td>Cardiac MIBG or fluorodopamine positron emission tomography (PET) scan</td>
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<tr>
<td>Hypotension-induced vasopressin release</td>
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<td>Hypotensive response to trimethaphan</td>
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<td>Pressor response to yohimbine</td>
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<td>Pressor response to droxidopa</td>
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<tr>
<td>Pressor response to atomoxetine</td>
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</tbody>
</table>

MIBG = metaiodobenzylguanidine.
* Diabetes mellitus, Parkinson disease, pure autonomic failure, dementia with Lewy bodies, amyloidosis, autoimmune and other causes of autonomic neuropathy.
patient’s hematocrit returns to normal levels. Lower maintenance doses (25 U/kg 3 times a week) may then be used. Concurrent iron supplementation is typically required during the period when the hematocrit is increasing.

**SYMPATHETIC ENHANCEMENT.** Commonly used pharmacologic strategies to induce vasoconstriction and increase peripheral vascular resistance include the \(\alpha\)-adrenoceptor agonist midodrine, the norepinephrine precursor droxidopa, and norepinephrine reuptake inhibitors.

**MIDODRINE.** Midodrine is an oral prodrug converted peripherally into the active metabolite desglymidodrine, a selective \(\alpha\)-adrenoceptor agonist that constricts arteriolar and venous vasculature, thus increasing blood pressure. The FDA approved midodrine in 1996 for the treatment of symptomatic orthostatic hypotension after clinical trials showed efficacy to increase standing blood pressure and improve orthostatic tolerance.\(^{70}\) As with other drugs for orthostatic hypotension, administration of midodrine increases blood pressure in all positions. In contrast to fludrocortisone, midodrine is a short-acting agent. Standing systolic blood pressure increases by 10 mm Hg to 30 mm Hg approximately 1 hour after a 10-mg dose, with some effect persisting up to 3 hours. Treatment should begin with 2.5 mg or 5 mg, which can then be increased up to 10 mg 3 times a day. As with other pressor agents, supine hypertension is common with midodrine; hence, patients should not take it within 3 to 4 hours before bedtime. Other common side effects are piloerection (goose bumps), scalp itching, and urinary retention. Midodrine has no effect on heart rate as it does not stimulate cardiac \(\beta\)-adrenergic receptors and, owing to its poor diffusion across the blood-brain barrier, has no CNS side effects.

**DROXIDOPA.** Droxidopa is an oral synthetic amino acid that converts to norepinephrine.\(^{71}\) Droxidopa is decarboxylated to norepinephrine by the enzyme aromatic L-amino acid decarboxylase, the same enzyme that converts levodopa to dopamine. Conversion of droxidopa to norepinephrine occurs in the remaining sympathetic postganglionic terminals as well as in non-neuronal tissues, particularly the kidney.\(^{72}\) Droxidopa was approved in Japan in 1989 for the treatment of neurogenic orthostatic hypotension in hereditary amyloidosis, Parkinson disease, and multiple system atrophy.\(^{71}\) The FDA approved droxidopa in 2014 after clinical trials showed its efficacy to improve symptoms of orthostatic dizziness, lightheadedness, or “feeling about to faint” in adult patients with symptomatic neurogenic orthostatic hypotension caused by Parkinson disease, multiple system atrophy, pure autonomic failure, and other rare disorders affecting norepinephrine production, such as dopamine \(\beta\)-hydroxylase deficiency characterized by defective norepinephrine release from sympathetic nerves upon standing.\(^{73-76}\)

Similar to midodrine, droxidopa is a short-acting agent (FIGURE 9-4).\(^{77,78}\) The peak pressor response occurs within approximately 3.5 hours after oral administration. The recommended dosage varies from 100 mg to 600 mg up to 3 times a day. To identify the best dose for each patient, supervised titration by a clinician is recommended.\(^{79,80}\) Although in clinical trials droxidopa was administered 3 times a day, clinical experience shows that the dose of droxidopa should be individualized to each patient’s needs, taking into account when the patient is standing and active. For example, in a patient with a movement
disorder and orthostatic hypotension who is active for only a few hours in the morning (eg, showering, preparing breakfast), it is reasonable to use a single morning droxidopa dose and skip the afternoon and evening doses. Other patients with different needs may receive droxidopa only 2 times a day or take a higher dose in the morning with lower doses in the afternoon and evening. The most robust pressor response occurs in patients with low plasma norepinephrine levels, indicating loss of peripheral sympathetic neurons.65 A supine plasma norepinephrine level lower than 220 pg/mL in patients with neurogenic orthostatic hypotension has high sensitivity and specificity to predict a pressor response to droxidopa.65

Droxidopa may be less effective in patients with neurogenic orthostatic hypotension and parkinsonism receiving high dosages of carbidopa (higher than 200 mg/d) as carbidopa blocks the conversion of droxidopa to norepinephrine.75,76,78,79 The most common side effects of droxidopa are hypertension, headache, and nausea. Although no specific studies have been done, concomitant use of droxidopa with norepinephrine reuptake inhibitors (eg, atomoxetine, venlafaxine) or adrenergic agonists (eg, midodrine) may enhance the pressor effect; caution is advised.

NOREPINEPHRINE REUPTAKE INHIBITORS. An emerging approach in the treatment of neurogenic orthostatic hypotension is the use of inhibitors of the norepinephrine membrane transporter, which inhibit norepinephrine reuptake and increase its availability in the neurovascular junction.

FIGURE 9-4
Pressor effect of midodrine and droxidopa versus placebo. Midodrine (A) and droxidopa (B) have a similar short-acting pressor effect profile. Both medications have a fast pressor effect beginning approximately 1 hour after oral administration (green arrows). The pressor effect of midodrine remains for 4 to 5 hours, whereas the pressor effect of droxidopa is slightly longer at 5 to 6 hours. The peak standing systolic blood pressure occurs 1 hour after midodrine administration, whereas the peak standing mean blood pressure occurs 3.5 hours after droxidopa administration.


KEY POINTS
- Determining the site of the autonomic lesion (central versus peripheral) in patients with neurogenic orthostatic hypotension has important therapeutic implications. Patients with central autonomic dysfunction (ie, decentralization) have a more pronounced pressor response to norepinephrine reuptake inhibitors, whereas patients with peripheral autonomic dysfunction (ie, denervation) have a more pronounced pressor response to norepinephrine enhancers and agonists.
- For patients who still remain symptomatic despite nonpharmacologic measures, stepwise pharmacologic treatment begins with low-dose fludrocortisone (0.1 mg/d), particularly in patients with volume depletion.
- Frequently used fludrocortisone dosages range from 0.05 mg/d to 0.2 mg/d. There is little benefit in increasing fludrocortisone to dosages higher than 0.2 mg/d. Common short-term side effects include hypokalemia; long-term side effects include left ventricular hypertrophy and renal failure.
- In patients with anemia of chronic disease and orthostatic hypotension, subcutaneous recombinant human erythropoietin increases blood pressure and improves orthostatic tolerance.
- When starting droxidopa, a careful titration is required to identify the best dose for each patient and prevent excessive supine hypertension.
In healthy subjects, norepinephrine reuptake inhibition has little effect on blood pressure. Although norepinephrine reuptake inhibitors enhance noradrenergic vasoconstriction at the level of the sympathetic postganglionic fibers, this is counteracted by norepinephrine-mediated stimulation of central \( \alpha_2 \)-receptors in the CNS, which has a vasodilator effect. However, in patients with central autonomic dysfunction, norepinephrine reuptake inhibitors result in only peripheral vasoconstriction, making them particularly suitable for patients with multiple system atrophy.

Short-term controlled clinical trials have shown that atomoxetine (10 mg to 18 mg, 2 times a day), a short-acting norepinephrine reuptake inhibitor, increases standing blood pressure and reduces the burden of symptoms compared to placebo in patients with neurogenic orthostatic hypotension.81–83

**CASE 9-2**
A 68-year-old woman with Parkinson disease presented with a 9-month history of dizziness, lightheadedness, and shortness of breath after walking for 100 yards and climbing stairs. She had been diagnosed with Parkinson disease 2 years earlier and was taking carbidopa/levodopa 25 mg/100 mg 3 times a day with excellent response and remaining very active.

Her blood pressure in the supine position was 148/92 mm Hg with a heart rate of 69 beats/min. After 3 minutes in the standing position, her blood pressure was 84/59 mm Hg with a heart rate of 71 beats/min (change in heart rate [\( \Delta HR \)]/change in systolic blood pressure [\( \Delta SBP \)] ratio of 0.03 beats per minute/mm Hg), and she reported feeling severely dizzy and lightheaded (FIGURE 9-5). ECG, complete blood cell count, and metabolic panel were normal. Autonomic testing confirmed neurogenic orthostatic hypotension with plasma norepinephrine levels of 102 pg/mL when supine and 138 pg/mL when standing.

She was educated on nonpharmacologic measures, including liberalization of salt and water intake, wearing compression garments (waist-high stockings), and sleeping with the head of the bed raised 30 to 45 degrees with the help of an electric bed or mattress.

She returned 2 months later reporting symptomatic improvement, although she still reported dizziness when standing for a few minutes. Her blood pressure in the supine position was 147/82 mm Hg with a heart rate of 69 beats/min. After 3 minutes in the standing position, her blood pressure was 91/79 mm Hg with a heart rate of 72 beats/min, and she reported feeling moderately dizzy and lightheaded.

Based on her low plasma norepinephrine levels indicating postganglionic sympathetic denervation, an in-office titration with droxidopa was performed, after which the patient was started on 300 mg 3 times a day and reminded to avoid the supine position and sleep with the head of the bed raised 30 to 45 degrees. She returned 1 month later reporting a significant abatement in her symptoms. Her blood pressure in the supine position was 151/92 mm Hg with a heart rate of 68 beats/min. After 3 minutes in the standing position, her blood pressure was 101/81 mm Hg with a heart rate of 72 beats/min and she remained asymptomatic.
the norepinephrine level, the greater the pressor effect and symptomatic improvement with atomoxetine, which makes it a particularly attractive option for patients with neurogenic orthostatic hypotension caused by autonomic decentralization (eg, multiple system atrophy). A multicenter controlled trial to confirm the efficacy of atomoxetine in patients with neurogenic orthostatic hypotension is under way. A phase 2 trial with ampreloxetine (TD-9855), a long-acting investigational norepinephrine reuptake inhibitor, showed that this compound was safe and increased blood pressure and orthostatic tolerance in patients with neurogenic orthostatic hypotension; a large multicenter phase 3 study to confirm its efficacy is ongoing.

Conversely, lower supine plasma norepinephrine levels appear to predict a greater symptomatic and pressor response to droxidopa, a synthetic oral

**FIGURE 9-5**

Blood pressure and heart rate of the patient in CASE 9-2 supine and standing. The tracing shows severe orthostatic hypotension with no compensatory increase in heart rate, with a change in heart rate (ΔHR)/change in systolic blood pressure (ΔSBP) ratio below 0.5 beats per minute/mm Hg, indicative of neurogenic orthostatic hypotension.

Symptomatic neurogenic orthostatic hypotension afflicts approximately 20% of patients with Parkinson disease. The neurogenic origin of orthostatic hypotension was confirmed in this patient by a ΔHR/ΔSBP ratio below 0.5 beats per minute/mm Hg and a blunted norepinephrine release when standing up. The stepwise approach for patients with neurogenic orthostatic hypotension begins with nonpharmacologic measures and, when these are not sufficient, implementing pharmacologic therapy. Droxidopa, a synthetic norepinephrine precursor, was expected to produce a pressor response in this patient given her low plasma norepinephrine levels indicative of peripheral sympathetic denervation, and as anticipated, it resulted in significant symptomatic improvement.
CASE 9-3

A 63-year-old man presented for evaluation 10 days after an episode of brief unresponsiveness and collapse. After a large and typical Thanksgiving dinner, he stood up, walked a few steps, and suddenly collapsed to the floor. He was unresponsive but came to in a few seconds, startled but not confused. His wife was with him and reported that he had no involuntary movements, loss of urine, or tongue biting. He was taken by ambulance to a local hospital, where his blood pressure was 160/95 mm Hg. ECG, echocardiogram, complete blood cell count, metabolic panel, urinalysis, and a 24-hour Holter monitor were normal. He was diagnosed at that hospital with arterial hypertension, and antihypertensive treatment was recommended, which he did not take.

On questioning during the current visit, he recalled having brief episodes of mild lightheadedness and blurry vision when standing up after meals, mostly after breakfast, for about 2 years. His wife measured his blood pressure on one of these occasions, and it was approximately 80/60 mm Hg. His symptoms abated after sitting or lying down, and he had never lost consciousness until the episode that took him to the hospital. He reported moderate constipation, erectile dysfunction, and nocturia.

On physical examination, he appeared healthy. He had preserved cognition, intact cranial nerves, normal deep tendon reflexes, flexor plantar responses, and no sensory deficits. His supine blood pressure was 157/102 mm Hg with a heart rate of 72 beats/min and after standing for 3 minutes was 119/75 mm Hg with a heart rate of 79 beats/min (change in heart rate [ΔHR]/change in systolic blood pressure [ΔSBP] ratio of 0.18 beats per minute/mm Hg). He had no orthostatic symptoms in the office.

He was given an ambulatory 24-hour blood pressure monitor, which showed symptomatic drops in blood pressure associated with breakfast, lunch, and dinner, consistent with postprandial hypotension (FIGURE 9-6). After these findings were reviewed, the patient was contacted over the phone and instructed to eat smaller and more frequent meals, to decrease carbohydrate-rich meals during daytime, and to start taking acarbose 100 mg before breakfast, lunch, and dinner for the off-label indication of lessening his postprandial hypotension. He was instructed to recognize symptoms of orthostatic hypotension, to quickly sit down to prevent syncope, and to follow nonpharmacologic measures to increase his orthostatic tolerance. One month later, the patient came for a follow-up visit reporting marked improvement in his postprandial symptoms.
This patient had asymptomatic neurogenic orthostatic hypotension in the office (his blood pressure fell 38/27 mm Hg and his ΔHR/ΔSBP ratio was below 0.5 beats per minute/mm Hg) with supine hypertension. He became symptomatic only after meals, consistent with postprandial hypotension. His autonomic failure (orthostatic hypotension, constipation, erectile dysfunction, bladder dysfunction) in the absence of motor or sensory deficits is suggestive of pure autonomic failure. Treatment of postprandial hypotension includes reducing high glycemic index carbohydrates, eating smaller and more frequent meals, and using the α-glucosidase inhibitor acarbose. These patients require close follow-up as they may develop worsening symptoms of orthostatic hypotension at times other than after meals.
norepinephrine precursor. These responses can be explained by denervation supersensitivity of adrenergic receptors. Consequently, patients with low plasma norepinephrine levels (usually seen in Lewy body disorders [CASE 9-2] or peripheral autonomic neuropathies) may respond better to droxidopa and midodrine, whereas patients with normal or high norepinephrine levels (usually multiple system atrophy) may respond better to norepinephrine reuptake inhibitors.

In patients with refractory neurogenic orthostatic hypotension, norepinephrine reuptake inhibition could theoretically be combined with droxidopa or midodrine, with or without fludrocortisone or pyridostigmine. However, no safety data are available on the combined use of most of these agents, and extreme caution is advised.

OTHER MEDICATIONS. Pyridostigmine, a cholinesterase inhibitor, enhances cholinergic neurotransmission in sympathetic and parasympathetic ganglia. A double-blind study showed that pyridostigmine increases systolic blood pressure, on average, by only 4 mm Hg. The combination of 5 mg midodrine with 60 mg pyridostigmine was slightly more effective than pyridostigmine alone. Similarly, the combination of pyridostigmine with atomoxetine appears to have a synergistic effect to increase blood pressure and improve orthostatic tolerance.

POSTPRANDIAL HYPOTENSION
Hypotension after meals regularly occurs in patients with sympathetic failure and can be its only manifestation, even in patients without overt orthostatic hypotension. Postprandial hypotension is defined as a fall of at least 10 mm Hg in systolic blood pressure within 2 hours of eating. Management starts by eating smaller and more frequent meals with low carbohydrate content and avoiding alcohol. Drugs that delay or block the release of insulin, a known vasodilator, such as the α-glucosidase inhibitor acarbose (50 mg to 100 mg before meals), decrease gastrointestinal absorption of glucose and are useful to treat postprandial hypotension (CASE 9-3). Midodrine taken right before or during meals may also help. The somatostatin analogue octreotide induces vasoconstriction of splanchnic vessels; it is administered subcutaneously (0.2 mcg/kg to 0.4 mcg/kg) and is very effective to attenuate postprandial hypotension, although it can induce nausea and abdominal pain.

NEUROGENIC SUPINE HYPERTENSION
The prevalence of neurogenic supine hypertension is 30% to 50% in Parkinson disease, 40% in multiple system atrophy, and 50% to 70% in pure autonomic failure. The frequency of neurogenic supine hypertension in diabetes mellitus and amyloid neuropathy is unknown.

Treatment of supine hypertension focuses on reducing blood pressure to lower the risk of target organ damage without worsening hypotension. Achieving this goal is challenging. Patients should avoid the supine position. For daytime naps, patients should sit in a reclining chair with their feet on the floor. At night, tilting the head of the bed to a 30- or 45-degree angle lowers blood pressure. This is best accomplished with an electric bed or mattress. A carbohydrate-rich snack or an alcoholic drink before bedtime lowers blood pressure. The application of an abdominal heating pad to lower blood pressure by inducing splanchnic vasodilation is being currently studied in a clinical trial.
In patients with severe prolonged supine hypertension at night despite elevation of the head of the bed (systolic blood pressure of at least 180 mm Hg or diastolic blood pressure of at least 110 mm Hg), short-acting antihypertensives (eg, captopril 25 mg, losartan 50 mg, or nitroglycerin patch 0.1 mg/h) at bedtime could be considered, particularly in patients who already have target organ damage, although none of these approaches has been studied in large controlled trials.94–96 Patients should be advised about the augmented risk of hypotension and falls if they stand up at nighttime (eg, to urinate). To avoid this, the use of a urinal or bedside commode should be encouraged.

CONCLUSION
Orthostatic hypotension is a disabling disorder that occurs frequently in the elderly as a consequence of drug effects, volume depletion, or cardiovascular deconditioning. Neurogenic orthostatic hypotension is common in patients with diseases affecting central or peripheral sympathetic neurons. Patients with orthostatic hypotension with no or minor symptoms can be treated with nonpharmacologic measures only. Patients with a moderate burden of symptoms typically require a combination of nonpharmacologic and pharmacologic therapies (eg, the synthetic mineralocorticoid fludrocortisone and the pressor agents midodrine, droxidopa, or atomoxetine).

REFERENCES

KEY POINTS
● Treatment with norepinephrine reuptake inhibition is emerging as a potentially effective option for patients with neurogenic orthostatic hypotension, particularly those with autonomic dysfunction from damage to the central nervous system (eg, decentralization).
● Pyridostigmine alone has little effect to increase blood pressure. It appears to have synergistic effects when combined with midodrine or atomoxetine.
● Neurogenic supine hypertension is best treated with postural measures, ie, avoiding the flat position and sleeping with the head of the bed raised 30 to 45 degrees with the help of an electric bed or mattress. In patients with refractory supine hypertension and high risk of organ damage, short-acting antihypertensives at bedtime might be considered.


MANAGEMENT OF ORTHOSTATIC HYPOTENSION


69 Grijaiva CG, Biaggioni I, Griffin MR, Shibao CA. Fludrocortisone is associated with a higher risk of all-cause hospitalizations compared with midodrine in patients with orthostatic hypotension. J Am Heart Assoc 2017;6 pii: e006848. doi:10.1161/JAHA.117.006848.


DISCLOSURE

Continued from page 154

the Familial Dysautonomia Foundation, Inc; the Michael J. Fox Foundation for Parkinson’s Research; the Multiple System Atrophy Coalition; the National Institutes of Health (R01HL103988, U54NS065756); Theravance Biopharma, and the US Food and Drug Administration (FDK3731-01) and publishing royalties from UpToDate, Inc. Dr Kaufmann has served as an expert witness for the Department of Justice regarding the alleged relationship between human papilloma virus vaccination and autonomic disorders.
Orthostatic hypotension (OH) is very common in older people and is encountered daily in emergency departments and medical admissions units. It is associated with a higher risk of falls, fractures, dementia and death, so prompt recognition and treatment are essential. In this review article, we describe the physiology of standing (orthostasis) and the pathophysiology of orthostatic hypotension. We focus particularly on aspects pertinent to older people. We review the evidence and consensus management guidelines for all aspects of management. We also tackle the challenge of concomitant orthostatic hypotension and supine hypertension, providing a treatment overview as well as practical suggestions for management. In summary, orthostatic hypotension (and associated supine hypertension) are common, dangerous and disabling, but adherence to simple structures management strategies can result in major improvements.

KEYWORDS: orthostatic hypotension, older, supine hypertension, postural hypotension, orthostasis

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Introduction

Orthostatic hypotension (OH) is common in older people and is encountered daily by emergency and general physicians. Defined by a drop of >20 mmHg in systolic blood pressure (BP) or >10 mmHg diastolic BP after standing for three minutes, it is seen in almost a quarter (24%) of emergency department (ED) presentations with syncope, a fifth (19%) of older trauma inpatients and 68% of older general medicine inpatients.1–3 It is a persistent problem: Hospital Episode Statistics show that admissions resulting from OH have risen dramatically over the last decade.4

OH is neither incidental nor benign. It is associated with a higher risk of coronary artery disease, myocardial infarction, stroke, falls, fracture, road accidents and death.5–8 A sustained reduction in systolic BP on standing is an independent risk factor for death with a 45% 5-year mortality.9 Furthermore, the diagnosis can be overlooked when patients with delayed OH are unaware of their reduced cerebral perfusion, reporting falls rather than dizziness or syncope.

It is thus essential that it is identified, and that the consequences are anticipated and managed. In this review article, we outline the pathophysiology of OH, along with specific associations to consider in older people. We then detail the management principles and emerging evidence.

Pathophysiology of OH in older people

When a human stands up, 500–1,000 mL blood pools from the thoracic cavity to the legs, buttocks, abdomen and pelvis. Blood in the abdomen pools in the splanchnic vascular bed which can contain a quarter of the body’s blood at any time (Fig 1).10–12 To compound this, plasma volume decreases by 10–15% as fluid from the plasma shifts into the interstitial spaces in the lower legs from osmotic forces. As a result of this redistributed plasma volume, there is lower venous return to the heart. Consequently, the pressure in the right atrium falls, right ventricular filling falls, leading to reduced stroke volume and, ultimately, lower cardiac output.10–12

The body’s response to standing (orthostasis) is finely regulated. Walking, involuntary postural sway and voluntary leg muscle contraction act as a pump (aided by venous valves) and propel significant volumes of blood towards the heart.10–12 The autonomic nervous system (ANS) also plays a role. The reduction in venous return to the heart and the subsequent fall in cardiac output is detected by the baroreceptors in the aortic arch and carotid sinus, and the venoatrial stretch receptors in the heart and lungs. On sensing the lower arterial pressure, these baroreceptors send signals to the brain to increase sympathetic outflow. This, in turn, induces peripheral vasoconstriction, splanchnic vasoconstriction and increases plasma noradrenaline release from sympathetic neurons. Consequently, the heart rate increases and, to a lesser extent, stroke volume also increases, given normal cardiac function. The renal angiotensin system is activated by
the reduced plasma volume, leading to vasopressin release which contributes to vasoconstriction and increases plasma volume.\textsuperscript{10,12}

In neurogenic OH (Fig 2), the baroreflex is impaired, and these compensatory mechanisms do not occur, most obviously with a lack of increase in heart rate. Hypotension ensues, with persistent reduction in cardiac output. Unless this is corrected by sitting or lying supine, cerebral hypoperfusion and syncope may ensue. Neurogenic OH results from impairment at multiple levels of the autonomic nervous system: from the brain and spinal cord to the pre- and post-ganglionic sympathetic and parasympathetic nervous systems, down to the peripheral autonomic nerves. The commonest cause in older people is the group of neurodegenerative disorders known as the synucleinopathies. This group includes Parkinson’s disease (PD), dementia with Lewy bodies (DLB), multi-system atrophy (MSA) and primary autonomic failure. In PD (which confers a relative risk of 7 for OH as the disease progresses) and DLB, the dorsal motor nucleus of vagus is most likely to be affected.\textsuperscript{13} Lesions of peripheral autonomic nerves can be caused by diabetes, HIV, amyloidosis, autoimmune and paraneoplastic processes.\textsuperscript{10,11,14} OH is present in around a third of diabetic patients, particularly in individuals with other end organ damage (such as peripheral neuropathy) and is associated with higher mortality.\textsuperscript{15}

**OH associations pertinent to older people**

**Age-related changes to the autonomic nervous system**

Changes in the ANS and baroreflex are associated with ageing. Baroreceptor sensitivity is reduced in older patients, possibly due to atherosclerosis. As a result, appropriate compensatory mechanisms on orthostasis may not occur.\textsuperscript{16,17} Additionally the heart rate component of the baroreflex and the sympathetic control of muscle activity may be impaired.\textsuperscript{18,19}

**Bedrest and immobility**

Immobility and associated deconditioning are major causes of OH. A vicious cycle can develop, where OH leads to further immobility. Physical activity levels decline significantly after 70 years, even in healthy people.\textsuperscript{20} Activity levels in older inpatients are very low, even with physiotherapy.\textsuperscript{21}

The physiological effects of prolonged bed rest have been well studied, as head-down bedrest are used as a model for investigating the effects of chronic weightlessness in space travel. Prolonged bedrest decreases plasma volume and total body blood volume, impairs baroreflex adjustment, reduces cardiac output, and stroke volume, and inhibits sympathetic nerve responses.\textsuperscript{22–25}

**Drugs**

Drug-induced OH is the most common reason for presentation to ED with OH.\textsuperscript{7} Being on multiple drugs confers a higher risk.\textsuperscript{26} Particular culprits are selective serotonin reuptake inhibitors with an odds ratio (OR) of 2.42 for developing OH, selective noradrenaline reuptake inhibitors (OR 5.37), tricyclic antidepressants, calcium channel blockers (OR 1.79) and benzodiazepines.\textsuperscript{26–29} Excess alcohol use is also associated with an increased risk (OR 2.17) possibly due to autonomic neuropathy.\textsuperscript{27}
Arterial stiffness

Arterial stiffness, a biomarker of coronary artery disease and vascular ageing, positively correlates with OH independent of whether hypertension is present. Even in middle age, arterial stiffness correlates with an impaired autonomic response to standing. Additionally, individuals with atrial fibrillation are more likely to have OH, likely due to higher burden of vascular pathology.

Frailty

Frailty levels are positively correlated with OH and orthostatic intolerance symptoms, even without postural BP changes. Frailty also increases the risk of mortality, disability, functional decline and hospitalisation in individuals with OH.

Delayed heart rate recovery on standing

The Irish Longitudinal Study on Ageing (TILDA) has shown that failure to recover heart rate after standing when assessed by beat-to-beat monitoring is common and often asymptomatic. Nevertheless, it carries an adverse cardiovascular prognosis and is associated with OH, falls and polypharmacy.

Cognitive impairment

OH is associated with cognitive decline and dementia. One meta-analysis estimates an increased dementia risk of 21%. In a memory clinic cohort, OH correlated with the severity of cognitive deficits, particularly executive function.

Individuals with OH have increased white matter hyperintensity volume on magnetic resonance imaging (MRI) and faster cognitive deterioration rates. Additionally, the magnitude of OH correlates with white matter hyperintensity volume in depressed older people. This suggests altered haemodynamics and reduced cerebral perfusion. In patients with both mild cognitive impairment and Parkinson’s disease, having OH increases the conversion risk to dementia. This could be caused by repetitive reduction in brain perfusion. Alternatively, it could reflect wider changes in the central and autonomic nervous systems in the synucleinopathies.

Diagnosis

The ‘active stand test’ involves measuring BP while supine, on standing and then after standing for 3 minutes. This may inform about immediate OH (OH within 3 minutes) and classical OH (OH at 3 minutes) but will not assess delayed OH (occurring after 3 minutes). Clinicians should be aware that patients with delayed OH may be unaware of their reduced cerebral perfusion and may present as falling, rather than dizziness or syncope.

Even more valuable is the active stand test with continuous electrocardiography (ECG) and beat-to-beat BP using a non-invasive photoplethysmographic device on the finger or wrist. This method will clearly show what happens to BP in the erect posture.

Other tests of value are notably the Valsalva manoeuvre which stresses the autonomic nervous system which, in neurogenic OH, indicates the lack of heart rate rise that should occur. Twenty-four-hour ambulatory BP monitoring is also valuable in assessing the
Management of orthostatic hypotension

General principles

The aim of management is to reduce symptoms and improving standing time, physical function and activity. This takes precedence over optimising standing BP.\textsuperscript{52} An essential facet is patient education. Patients should be advised on hydration and diet, and to avoid triggers such as hot environments.\textsuperscript{1,53} Large carbohydrate-rich meals should be avoided because post-prandial hypotension can exacerbate symptoms.\textsuperscript{1} A medication review should occur with beta-blockers, thiazides, nitrates neuroleptics and dopaminergic agents under particular consideration.\textsuperscript{53,54} Individualised physical exercise regimens to combat deconditioning should be encouraged.\textsuperscript{1,53} Some consensus guidelines suggest avoiding orthostatic exercises and opting for horizontal exercise such as rowing machines, swimming and exercise bikes.\textsuperscript{53}

During general assessment, anaemia, thyroid disorders, and vitamin D and B12 deficiencies should be corrected as these can contribute to and exacerbate OH.\textsuperscript{53,55}

Patients should be advised to measure their blood pressure at home and keep a diary detailing activities, fluid and salt intake, blood pressure readings and symptoms.

A summary of management is shown in Table 1.

Non-pharmacological measures

Expand plasma volume: aim for fluid repletion

Drinking water is an easy and effective way to improve BP.\textsuperscript{56} However, lack of thirst in this age group should be considered. Mechanisms can be independent of the fluid itself and are due to increased sympathetic activity resulting in a pressor effect.\textsuperscript{57}

The European Federation of Neurological Sciences (EFNS; now the European Academy of Neurology) suggests aiming for fluid repletion by drinking 2–2.5 L of fluid per day, and 500 mL bolus drinks when immediate rises in blood pressure are needed.\textsuperscript{1,58}

This may be undesirable for people with continence and mobility issues. Additionally, a fine balance needs to be considered for those limited by fluid restrictions (such as those with heart failure and chronic kidney disease).

Avoid venous pooling: teach physical manoeuvres

Leg exercises (such as squatting, knee and leg crossing) are effective at reducing lower body pooling and expelling blood upwards towards the heart, increasing venous return and improving BP.\textsuperscript{12} Caution should be applied in individuals with balance problems. Patients should be shown how to employ these measures at symptom onset (Fig 3).\textsuperscript{1,12}

Avoid venous pooling: compression garments

Compressing the venous beds in the abdomen and legs is also effective. Evidence is strongest for abdominal compression.\textsuperscript{59–61}

Table 1. Implications for practice: summary of the key principles of managing orthostatic hypotension and neurogenic supine hypertension

<table>
<thead>
<tr>
<th>Principle of management</th>
<th>Intervention</th>
</tr>
</thead>
<tbody>
<tr>
<td>General principles of management</td>
<td>Educate on avoiding triggers and encouraging self-management, such as patient diaries. Review medications. Treat anaemia, B12 deficiency, optimise causes of autonomic neuropathy (HIV/amyloidosis/diabetes).</td>
</tr>
<tr>
<td>Non-pharmacological measures</td>
<td>Aim for fluid repletion (2–2.5 L) and 500 mL bolus when needed. Aim for salt repletion (4–10 g/day). Prescribe compression garments to include abdominal compression. Teach physical counter-manoeuvres. Demonstrate head-up sleeping (by at least 10 degrees).</td>
</tr>
<tr>
<td>Pharmacological measures</td>
<td>Volume expanders: fludrocortisone Sympathomimetics: midodrine Alternative agents: droxidopa, atomoxetine and pyridostigmine</td>
</tr>
<tr>
<td>Managing OH and nSH</td>
<td>Advise taking a low-dose short-acting anti-hypertensive at night. Encourage a snack at night to induce post-prandial hypotension. Advise to avoid water and vasopressor agents at night.</td>
</tr>
</tbody>
</table>

Stockings should go as high as the waist to include abdominal compression.\textsuperscript{62} stockings lower than waist height are not effective.\textsuperscript{53}

Garments can be difficult to put on, and are not readily tolerated by many patients leading to variable compliance. Additionally, they are contraindicated in peripheral vascular disease, and require Ankle Brachial Pressure Index measurements prior to use.

Expand plasma volume: supplement dietary salt

Salt supplementation in patients with unexplained syncope significantly improves BP, orthostatic tolerance and baroreceptor sensitivity.\textsuperscript{63,64}

Consensus guidelines suggest salt supplementation, with recommendations ranging from 4–10 g per day to 8 g day, the latter by the ESC.\textsuperscript{1,53,55} Salt repletion can be confirmed by a urinary sodium excretion of over 100 mEq / 24 hours.\textsuperscript{53}

Decrease venous return to inhibit natriuresis: head-up sleeping

Head-up sleeping improves orthostatic hypotension and symptoms both alone and in combination with drugs.\textsuperscript{65–67} This position
Orthostatic hypotension in older people

maintains renin-angiotensin activation (maintaining plasma volume for the morning) and also avoid pressure natriuresis and hypovolaemia associated with supine hypertension. Expert guidelines suggest elevating the head of the bed by 15–23 cm higher than the foot of the bed. Where possible, sleeping with the whole bed tilted (for example inpatient hospital beds) can also reduce nocturnal hypotension by pooling blood in the lower half of the body at night.

Non-pharmacological measures can often be sufficient but, when they are not, medications can be considered. There are no head-to-head trials on which agents to use initially, but each case should be considered individually.

Pharmacological measures

Volume expanders

Fludrocortisone is a volume expander that works by increasing sodium and water absorption. It has been shown to benefit patients with OH. However, data suggesting a benefit are weak. It is not well tolerated in older people and discontinuation is common, usually after around 8 months. The main problem is that the effects are not long-lasting, and supine hypertension develops early. Fludrocortisone is associated with hospitalisation in patients with heart failure.

Consensus guidelines also recommend midodrine as monotherapy or combined therapy, avoiding night-time doses. Midodrine is short acting and, thus, should not exacerbate supine hypertension. It is contraindicated in severe heart disease, acute renal failure, phaeochromocytoma and thyrotoxicosis.

Other medications, not yet endorsed in guidelines

Droxidopa is a noradrenaline prodrug which significantly improves OH and quality of life, and significantly reduces falls. Unlike midodrine, it does not cause increased supine hypertension, but it should also be avoided at night. It is not currently not endorsed by the ESC due to insufficient evidence in 2018.

Pyridostigmine is a cholinesterase inhibitor which increases cholinergic transmission in sympathetic ganglia, increasing sympathetic response to standing upright. It requires some residual autonomic function and is associated with cholinergic side effects, but does not result in supine hypertension.

Octreotide is an analogue of somatostatin which inhibits vasodilatory gastrointestinal hormone release and plays a role in post-prandial hypotension. Desmopressin can be considered in nocturnal polyuria, and erythropoietin can be used in anaemia.

An age-old paradox: orthostatic hypotension and supine hypertension

Counter-intuitively, orthostatic hypotension and concomitant nocturnal (or neurogenic) supine hypertension (nSH) are very common: half of individuals with neurogenic OH will also have nSH. nSH is defined as BP greater than or equal to 140/90 mmHg after 5 minutes in the supine position. This may manifest as ‘reverse dipping’ (the severe form with nSH) or ‘non-dipping’ (the loss of normal physiological nocturnal dip in BP). Both are caused by the same underlying issues: baroreflex and sympathetic nervous system activation are impaired, and the renin-angiotensin-aldosterone pathway is altered. In nSH, increased supine venous return at night induces a pressure diuresis.
which can reduce circulating volume by up to 2 kg.\textsuperscript{58} This then aggravates OH in the morning, worsening daytime symptoms.\textsuperscript{58} This paradox leads to significant treatment dilemmas. Both require treatment, but treating each risks exacerbating the other. OH is associated with risks of falls and injuries, but untreated hypertension leads to cardiovascular and renal disease. Calculating risk scores (such as FRAX for fragility fracture) and avoiding the highest risk situation should guide decision making. There is little evidence in this area, but multiple consensus documents are available that suggest assessing and balancing risks and benefits.\textsuperscript{53,58,87} Consensus opinions suggest individualised intervention when systolic BPs reach 160–180 mmHg. In people with very high falls risk and severe postural BP drops, higher BPs should be permitted.\textsuperscript{53}

All consensus statements recommend practical conservative measures. The driving principles are to reduce venous return to the heart at night, avoiding pressure diuresis and resulting morning hypovolaemia. Caution should be taken in treating supine hypertension in individuals who wake up at night for micturition, as this may significantly increase risk of nocturnal falls.

- Avoid the supine position, and sleep with the head of the bed raised by at least 10 degrees or by 25 cm.
- Avoid fludrocortisone (due to long half-life), diuretics and long-acting hypertensives.
- Limit water intake at night to avoid natriuresis. Ideally, pressor agents (at lowest doses) should be used when needed rather than regularly to aid symptoms.\textsuperscript{55}

Monitoring and follow-up

Identifying ‘successful’ treatment involves assessing symptoms, falls, quality of life, side effects and BP changes. If one medication is tried without symptomatic benefit or has intolerable side effects, it should be replaced with another and re-reviewed. Drug doses should be titrated to lowest effective dose and reviewed regularly. Adhering to conservative measures is emphasised.\textsuperscript{53}

Conclusion

Orthostatic hypotension is a common, persistent and disabling condition which is encountered daily in general medical practice. It drastically impairs quality of life and results in rapid and progressive deconditioning and functional deterioration, often resulting in institutionalisation. When OH co-exists with supine hypertension, careful consideration of short- and medium-term risks should be balanced and discussed with the patient. Using simple, effective, practical measures to diagnose, monitor and alleviate it can have a major impact in maintaining independence in older people.\textsuperscript{55}

References


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