Orthostatic hypotension in older people: considerations, diagnosis and management

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ABSTRACT

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

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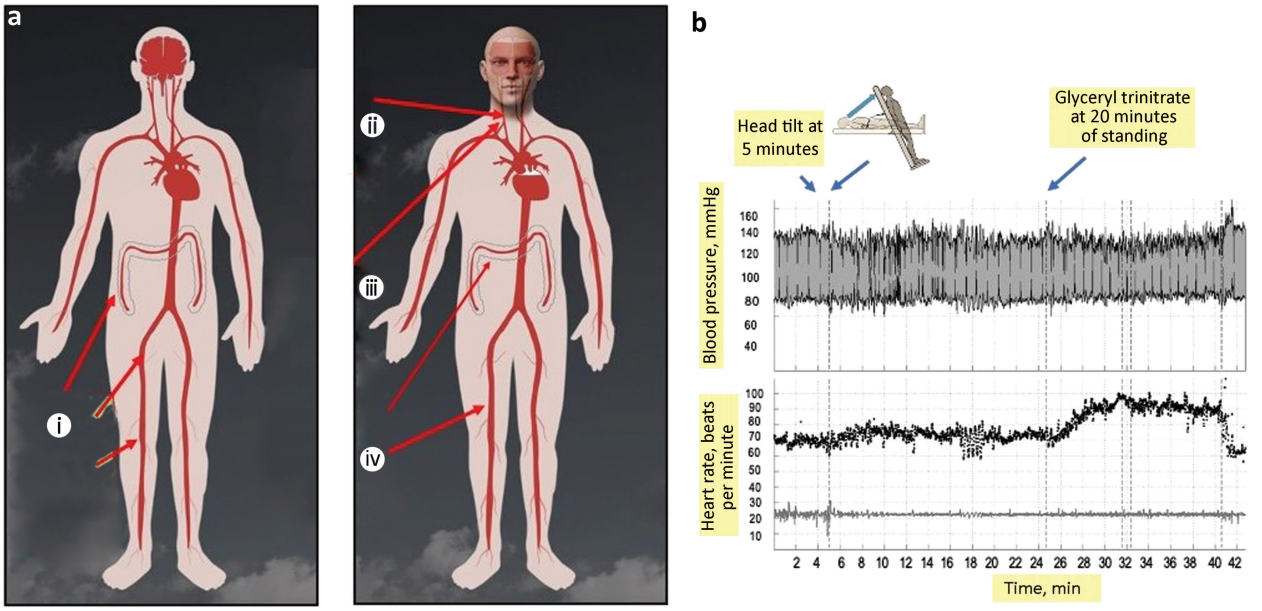

Fig 1. Normal haemodynamic changes on standing. a) i) Upon standing, blood pools in the legs, pelvis and gut, resulting in reduced venous return to the heart. ii) Baroreceptors in the aorta and carotid sinus, and mechanoceptors in the lungs and heart detect reduced venous return to the heart. iii and iv) Sympathetic nervous system activation releases noradrenaline into plasma with splanchnic/lower-limb vasoconstriction. The body's physiological response to standing is known as 'orthostasis'. Adapted with permission from Stop Fainting (www.stopfainting.com). b) Tilt table test: the heart rate (HR) and blood pressure (BP) reflect the normal haemodynamic response to standing on a tilt table. HR/BP are relatively stable on transition from lying to standing. A mild transient fall in BP occurs on reaching upright position, with a transient compensatory HR rise of ~15%.

the reduced plasma volume, leading to vasopressin release which contributes to vasoconstriction and increases plasma volume.[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.[13] Lesions of peripheral autonomic nerves can be caused by diabetes, HIV, amyloidosis, autoimmune and paraneoplastic processes.[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.[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.[16,17] Additionally the heart rate component of the baroreflex and the sympathetic control of muscle activity may be impaired.[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.[20] Activity levels in older inpatients are very low, even with physiotherapy.[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.[22–25]

Drugs

Drug-induced OH is the most common reason for presentation to ED with OH.[2] Being on multiple drugs confers a higher risk.[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.[26–28] Excess alcohol use is also associated with an increased risk (OR 2.17) possibly due to autonomic neuropathy.[27]

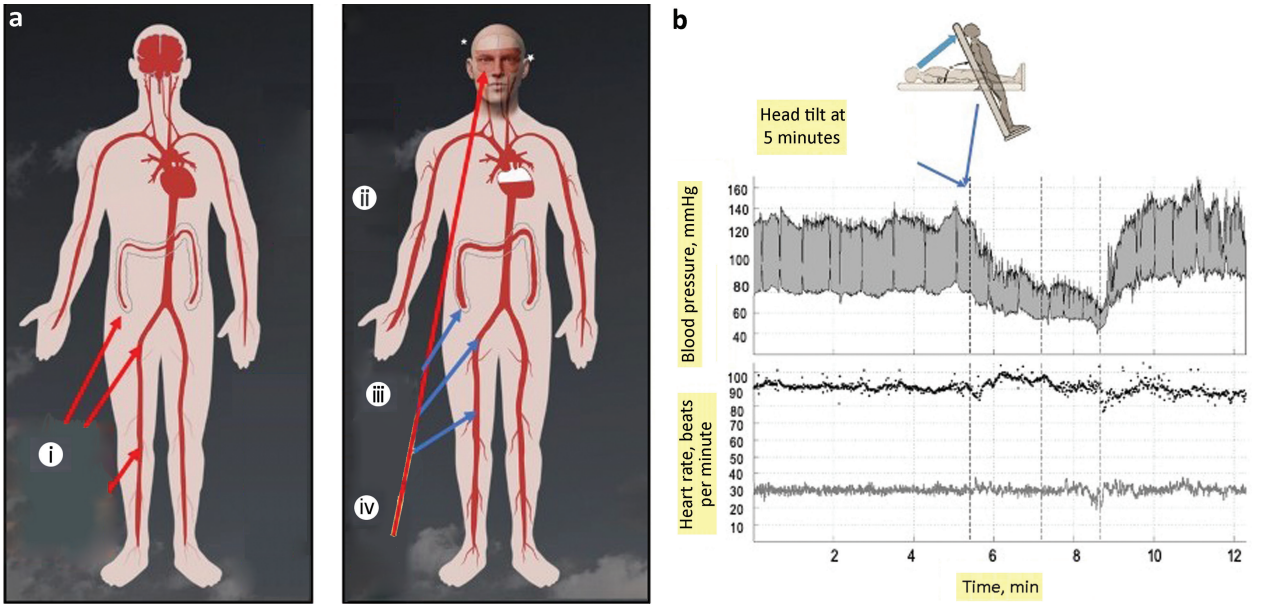

Fig 2. Haemodynamic changes occurring on standing in orthostatic hypotension. a) i) Upon standing, blood pools in the legs, pelvis and gut, resulting in reduced venous return to the heart. ii) Normal compensatory mechanisms for reduced venous return are absent. As a result, vasoconstriction does *not* occur and noradrenaline is not released into the circulation. iii) Blood continues to pool in the legs, pelvis and gut, leading to a further fall in venous return to the heart. iv) Brain hypoperfusion ensues and, unless the supine position is adopted, syncope occurs. Adapted with permission from Stop Fainting (www.stopfainting.com). b) Tilt table test: the heart rate and blood pressure reflect the physiological responses to standing on a tilt table. Following head-up tilt, the blood pressure falls until syncope is imminent at >10 minutes, at which point the supine position is resumed.

Arterial stiffness

Arterial stiffness, a biomarker of coronary artery disease and vascular ageing, positively correlates with OH independent of whether hypertension is present.[29–31] Even in middle age, arterial stiffness correlates with an impaired autonomic response to standing.[32] Additionally, individuals with atrial fibrillation are more likely to have OH, likely due to higher burden of vascular pathology.[33]

Frailty

Frailty levels are positively correlated with OH and orthostatic intolerance symptoms, even without postural BP changes.[34–38] Frailty also increases the risk of mortality, disability, functional decline and hospitalisation in individuals with OH.[39,40]

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.[41,42]

Cognitive impairment

OH is associated with cognitive decline and dementia.[43–47] One meta-analysis estimates an increased dementia risk of 21%.[43] In a memory clinic cohort, OH correlated with the severity of cognitive deficits, particularly executive function.[44]

Individuals with OH have increased white matter hyperintensity volume on magnetic resonance imaging (MRI) and faster cognitive deterioration rates.[48] Additionally, the magnitude of OH correlates with white matter hyperintensity volume in depressed older people.[49] 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.[50,51] 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

severity of the problem and detecting supine hypertension and post-prandial hypotension (for example, revealing blood pressure drops following mealtimes). Details of performance of these tests are available in the European Society of Cardiology (ESC) guidelines as an online supplement.[52]

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.[53] An essential facet is patient education. Patients should be advised on hydration and diet, and to avoid triggers such as hot environments.[1,53] Large carbohydrate-rich meals should be avoided because post-prandial hypotension can exacerbate symptoms.[1] A medication review should occur with beta-blockers, thiazides, nitrates neuroleptics and dopaminergic agents under particular consideration.[53,54] Individualised physical exercise regimens to combat deconditioning should be encouraged.[1,53] Some consensus guidelines suggest avoiding orthostatic exercises and opting for horizontal exercise such as rowing machines, swimming and exercise bikes.[53]

During general assessment, anaemia, thyroid disorders, and vitamin D and B12 deficiencies should be corrected as these can contribute to and exacerbate OH.[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.

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

Principle of management	Intervention
General principles of management	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).
Non-pharmacological measures	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).
Pharmacological measures	Volume expanders: fludrocortisone
	Sympathomimetics: midodrine
	Alternative agents: droxidopa, atomoxetine and pyridostigmine
Managing OH and nSH	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.

OH = orthostatic hypotension; nSH = neurogenic/nocturnal supine hypertension.

Non-pharmacological measures

Expand plasma volume: aim for fluid repletion

Drinking water is an easy and effective way to improve BP.[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.[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.[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. [12] Caution should be applied in individuals with balance problems. Patients should be shown how to employ these measures at symptom onset (Fig 3).[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.[59–61] Stockings should go as high as the waist to include abdominal compression.[62] Stockings lower than waist height are not effective.[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.[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.[1,53,54] Salt repletion can be confirmed by a urinary sodium excretion of over 100 mEq / 24 hours.[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.[65–67] This position

Fig 3. Physical counter-pressure manoeuvres. Patients should be educated on different physical counter-pressure manoeuvres to employ at the onset of symptoms on standing (a). Tensing lower body muscles while crossing arms and legs (b and c), raising a leg onto a raised surface (d) and squatting (e) can all increase venous return to the heart and raise blood pressure.

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.[53] Where possible, sleeping with the whole bed tilted (for example inpatient hospital beds) can also reduce nocturnal hypertension by pooling blood in the lower half of the body at night.[68]

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.[69,70] However, data suggesting a benefit are weak. It is not well tolerated in older people and discontinuation is common, usually after around 8 months.[71,72] The main problem is that the effects are not long-lasting, and supine hypertension develops early.[73] Fludrocortisone is associated with hospitalisation in patients with heart failure.[74] It should be avoided in cases of supine hypertension.

Sympathomimetics

Midodrine is an alpha-1 adrenoceptor agonist which increases BP by vasoconstriction.[1] It improves orthostatic tolerance and quality of life in OH and reflex syncope.[75–81] Side effects are supine hypertension, urinary retention and scalp itch due to pilomotor sensitivity.[79] It should be avoided in older males with prostatic symptoms. However, randomised control trials have shown that it is well tolerated and these side effects do not generally stop treatment.[76,81]

There is a significant risk of supine hypertension, so patients should be advised to avoid the supine position, avoid night-time doses and sleep head upright.[53] Combining midodrine with an abdominal binder can result in greater improvement than midodrine alone.[82]

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.[1,53]

Other medications, not yet endorsed in guidelines

Droxidopa is a noradrenaline prodrug which significantly improves OH and quality of life, and significantly reduces falls.[53,83–85] 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.[54]

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.[53]

Octreotide is an analogue of somatostatin which inhibits vasodilatory gastrointestinal hormone release and plays a role in post-prandial hypotension.[1] Desmopressin can be considered in nocturnal polyuria, and erythropoietin can be used in anaemia.[54] Finally, atomoxetine is as effective as midodrine in neurogenic OH in improving BP and has been shown to be superior in improving orthostatic intolerance symptoms.[86] It is not yet included in treatment guidelines.

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.[68] nSH is defined as BP greater than or equal to 140/90 mmHg after 5 minutes in the supine position.[68] This may manifest as 'reverse dipping' (the severe form with nSH) or 'non-dipping' (the loss of normal physiological nocturnal dip in BP). [14] 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.[58] This then aggravates OH in the morning, worsening daytime symptoms.[68]

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.[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.[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.
- Consider a low-dose, short-acting antihypertensive to ameliorate nocturnal hypertension.[58] Possible agents include a nitroglycerin patch, sildenafil, losartan, nebivolol, hydralazine, clonidine and nifedipine.[53,58]
- Have a snack before bedtime to induce post-prandial hypotension and reduce venous return to the heart.
- Ideally, pressor agents (at lowest doses) should be used when needed rather than regularly to aid symptoms.[14]

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.[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. ■

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