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TREATMENT OF ORTHOSTATIC HYPOTENSION IN OLDER PATIENTS: THE GERIATRIC PERSPECTIVE

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Abstract

Orthostatic hypotension (OH) is associated with increased co-morbid conditions in older patients. The treatment of orthostatic hypotension involves a multistep approach including identifying the cause and implementing interventions in the hopes of preventing fall-related trauma as well as increasing function and overall quality of life.

This article, the second of two articles on this topic, provides a description of both pharmacological and non-pharmacological interventions commonly employed in the treatment of orthostatic hypotension, including the rationale for when to employ specific treatments. The perspective of this paper is that of clinicians caring for frail seniors and consequently recommendations may be more cautious than in published guidelines. The paper focuses on recommendations that can be applied by generalist clinicians.

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postural hypotension, orthostatic, falls, fludrocortisone, midodrine

Key points

1. Treatment modalities are divided into non-pharmacological and pharmacological interventions. The latter are usually reserved for refractory cases that do not respond to non-pharmacological measures.
2. Non-pharmacological treatments include educating patients and their families on preventative strategies such as rising slowly to a standing position with support as well as avoiding risky situations or triggers such as hot environments and large meals, as these cause vasodilation that can worsen orthostatic hypotension.
3. Front-line pharmacological treatments predominantly include two drugs, fludrocortisone and midodrine, which should be used with caution and in cases of refractory OH. These medications require knowledge of and close monitoring of side effects.

Introduction

Orthostatic hypotension (OH), also known as postural hypotension, has been associated with an increased incidence of cardiovascular disease including coronary artery disease and stroke, as well as with the development of frailty and cognitive impairment in older persons.[1] OH is an independent predictor of falls and mortality.[2]

This article is the second in a two-part series on OH. The detection, measurement and diagnosis of causes of OH were reviewed in the first article in the series.[3] This second article focuses on treatment; both pharmacological and non-pharmacological interventions will be discussed, as will the rationale regarding when to employ specific treatments. The perspective of this paper is that of clinicians caring for frail seniors and consequently recommendations may be more cautious than in published guidelines. The paper focuses on recommendations that can be applied by generalist clinicians.

The case discussed in the first article by MacDonald[3] *et al*. will be presented again:

Mr. B. is a 72-year-old male who has been experiencing decreased appetite and multiple falls over the past several months. He was prescribed a cholinesterase inhibitor one year ago and was reassessed six months ago. His CT showed subcortical microangiopathic disease as well as evidence of lacunar strokes that he and his wife were unaware of. His MoCA at the time of diagnosis was 18/30, and for the past year his wife has been performing all instrumental activities of daily living and helping her husband with basic activities of daily living such as dressing.

Past medical history includes hypertension, type 2 diabetes with most recent HgA1c of 7.7 percent, coronary artery disease with a previous MI and ischemic cardiomyopathy with most recent LVEF of 32 percent seen on echocardiogram 18 months ago. He also has hypothyroidism and BPH. His medications include bisoprolol, perindopril, digoxin, furosemide, ASA, metformin, pantoprazole, levothyroxine, donepezil and tamsulosin. Review of systems reveals that Mr. B. has lost approximately 20 pounds over the past year as a result of decreased appetite. He does not recall his falls; his wife confirms that most occur when he is trying to get up to urinate during the night. Mrs. B. says she has no concerns during the day since her husband has been using the walker.

On physical exam, BMI is 20. Lying blood pressure is 120/62, HR 88 (regular rhythm). BP repeated in the standing position after one minute is 100/55, which confirms a diagnosis of orthostatic hypotension. He denies any symptoms of dizziness but does feel weak after standing for two minutes and requests to sit back down. He appears tremulous and is blinking his eyes and swaying, but still denies dizziness. Mucous membranes appear to be dry. Cardiovascular examination reveals no jugular venous distention and no peripheral edema.

He has a grade II/VI systolic ejection murmur best heard the left upper sternal border, which radiates to the right carotid area. Respiratory examination reveals clear lungs on auscultation. Abdomen is soft with no tenderness. MoCA is now 15/30 and his wife reports that the cholinesterase inhibitor has not slowed down the rate of cognitive decline.

Goals of treatment – when to treat OH and why

The prevalence of OH in community-dwellers aged 65 years and older is 16.2 percent and the incidence of OH increases exponentially with age[4]; this effect is increased with increasing number of prescribed medications and increasing prevalence of multiple comorbidities. The goal of treatment of OH should not be to achieve specific BP targets, but rather to improve symptoms, to optimize safety (reducing syncope and falls) and to maximize functional status.[5]

A systematic review by Logan *et al*. found that most randomized placebo-controlled trials of pharmacological and non-pharmacological treatment of OH are based on a small number of well-defined patients with primary forms of autonomic failure and hence may have limited generalizability.[6] Patients studied in these trials were not representative of the elderly population commonly seen with OH who often have multiple comorbidities and are on multiple contributing medications.

Treatment modalities are divided into (1) non-pharmacological measures and (2) pharmacological interventions. In patients without autonomic failure, treatment of the cause and reversal of the underlying deficit may be curative. This usually is not achievable in patients with autonomic failure, where a combination of non-pharmacological and pharmacological measures is often needed.[7]

Non-pharmacological measures

Non-pharmacological treatment is considered first line and may be sufficient as the sole treatment for many patients.

The first step after a thorough assessment (based on the 4D-AID approach) is to complete a full medication review and decrease or remove any potential medications that could cause or potentiate orthostatic hypotension – refer to Table 1 for a list of medication classes that cause OH (the 6As).

It is important to understand that antihypertensive therapy should not be abandoned in this patient population, but rather should be tailored to optimize BP control without causing falls due to OH. Adequate blood pressure control reduces the incidence of OH associated with hypertension.[8] Often it is not the dose of the medication but the rate of dose escalation that is the issue – slower up-titration of medications while monitoring for OH may prove helpful to balance the risks of hypertension (e.g., stroke, myocardial infarction) with the risk of postural hypotension (e.g., falls, fractures, traumatic brain injury) in order to optimize overall benefit to the patient. In some patients it may not be possible to fully achieve BP targets without placing them at risk of falls and trauma due to OH. The risk of high BP must be weighed against the risk of OH-associated falls in achieving the best possible balance for that particular patient. For more on BP management in medically complex seniors, see Can We Stay on Target?

Once a full medication review has been undertaken and possible contributors have been identified, the first step is to slowly wean down any potentially contributing medications that can be safely weaned and possibly discontinued.

While reviewing and optimizing medications (weaning contributors to OH) one can simultaneously begin educating patients and families. This involves teaching the triggers of OH and non-pharmacological interventions aimed at reducing venous pooling in the lower extremities thereby improving cardiac output.

1. Patient and family education

There is great merit in teaching patients and families what situations and times of day will lead to increased risk of OH. OH often occurs in the mornings; it is helpful to make patients and caregivers aware of this and, if this is the case, to suggest they plan exercises and activities in the afternoon. If mornings are times of predictable symptom worsening for a particular patient then extra caution and compensatory strategies (e.g., getting up slowly while holding on to solid furniture, maximizing fluids) can be employed at that time.

Patient surroundings including hot environments, hot baths or showers should be avoided or exposure minimized, as it has been shown that due to heat induced vasodilation of blood vessels patients experience greater postural drops in blood pressure in hot environments.[9] During times of intense environmental heat, there has been higher morbidity reported amongst those diagnosed with OH.[10]

There is also a phenomenon known as post-prandial hypotension; this is defined as a fall in systolic blood pressure of greater than 20 mmHg up to 90 minutes following a large sized meal. It is a condition associated with OH and is related to the rate of glucose entering the small intestine.[11,12] Once again, if this is a time of predictable symptom worsening for a particular patient then extra caution and compensatory strategies (e.g., getting up slowly while holding on to solid furniture and not ambulating immediately after meals) can be employed at that time. Help your patients and their caregivers predict times of increased risk and plan accordingly.

Alcohol can trigger OH and should be decreased, weaned off or avoided in patients with significant OH.

2. Behavioural techniques

Lifestyle modifications include advice to patients to avoid quick postural changes – patients should be advised to gradually move from supine to sitting to standing while monitoring for postural symptoms and holding on the stable objects (e.g., not a wheeled walker). If symptoms are too severe they may need to sit down until symptoms pass. It is also advised that patients and their families schedule any more strenuous activities in the afternoon when OH is not so common.

Head-up tilt at night (also referred to as reverse Trendelenburg) is strongly recommended in the literature for treatment of OH.[9] This is accomplished by using blocks to raise the head of the bed or a polystyrene wedge beneath the mattress. The bed is inclined at a 10-15 degree angle so that the head is higher than the pelvis and the leg is lower than hip. This improves OH through increasing plasma volume by reducing overnight diuresis. The mechanism is thought to work by the activation of the renin-angiotensin system due to lowered renal artery pressure.[13] See Figure 1. Some patients may not tolerate the head-up tilt.

Simple maneuvers such as leg-muscle pumping and tensing (i.e., contractions) to increase central venous return by pumping blood out of the lower extremities can bring on relief of symptoms associated with OH. Although this was shown in small case reports, it has rendered some benefit in those with OH.[9,14,15] For patients who cannot understand or follow contraction (pumping/tensing) of all leg muscles, pedal dorsiflexion (which only leads to contraction of muscles of lower leg) is often recommended.

3. Physical non-pharmacological interventions

Other non-pharmacological interventions include custom-fitted compression stockings – ideally thigh-high or waist-high. Compression stockings gently compress the legs and improve blood flow in the veins by preventing backward blood flow. Effective compression stockings apply the most amount of pressure at the ankle with decreasing pressure going upwards (i.e. creates a pressure differential/gradient or cone of pressure with higher pressure at the ankle and lower, albeit still significant, pressure higher up). Figure 2 and 3 illustrate this pressure gradient. Unfortunately, there are many challenges associated with these stockings. They are difficult to put on and can be hot and uncomfortable, which limits compliance. They can also be costly. It is important for clinicians to inspect the skin and peripheral pulses prior to this recommendation as these are contraindicated in patients with skin ulcers or peripheral arterial disease. If peripheral arterial disease is a concern then an Ankle-Brachial Index (ultrasound examination of arterial flow in legs) can be considered.

Other apparatus that have been shown in the management of OH include an abdominal binder. This can be easier to use than the compression stockings and may be equally as effective because the majority of the pooling is thought to occur in the splanchnic circulation where the binders apply about 20 mmHg of pressure.[3]

4. Water and salt

Most North Americans ingest 3-4 grams of salt per day. The American Heart Association guidelines recommend that the average salt consumption should not exceed 2 grams daily. In patients with significant OH these guidelines may not apply – it may be appropriate to at least permit 3-4 grams of salt per day if there are no significant contraindications such as CHF that easily decompensates. The systematic review by Shibao[2] indicated that patients with symptomatic OH may require added salt to increase plasma volume. In this review, it was recommended to increase salt consumption up to 6-10 grams daily assuming there were no contraindications present. We cannot recommend such high doses of salt but, in our own practices do liberalize salt intake and sometimes recommend adding salt to the diet in patients with significant OH, no supine hypertension and no significant cardiac dysfunction.

Other simple interventions include increasing fluid intake to two liters per day if there are no contraindications. If nocturia is an issue then the fluids should be ingested earlier in the day preferably before supper.

Malnutrition and dehydration are common in hospitalized patients. If there are no contraindications (e.g., heart failure, very low ejection fraction or significant diastolic dysfunction), consideration should be given to IV fluids to determine if postural hypotension can be rapidly and safely reversed.

5. Exercise

Prolonged bed rest leads to deconditioning which, in turn, can worsen OH. Exercise can counter this effect of deconditioning. There is, however, a cautionary note. Exercise can result in peripheral vasodilation, which can exacerbate OH. Consequently, in symptomatic patients, exercises should be chosen that minimize risk of falls and trauma. Examples of exercises that are helpful are water exercises (e.g., aquafit) which also cause improvement in venous return produced by the pressure of the water. Reclining exercises such as recumbent biking or rowing are preferable to upright ones such as the treadmill, which might create a fall risk. Exercise prevents deconditioning and further loss of muscle mass.[2]

Patients admitted to hospital are often confined to a bed with limited mobilization because of fear of them falling, thereby leading to *hospital-acquired deconditioning*, which contributes to OH. Patients should be encouraged to use a recliner or remain in a seated position for as long as possible during daytime hours. Safe and early mobilization with support should be encouraged to avoid *hospital-acquired disability*.

Pharmacological interventions

When OH is not relieved by traditional non-pharmacological interventions and patients remain at significant risk of falls and trauma, then pharmacologic agents are needed for treatment of symptomatic OH. These are typically added to non-pharmacological measures rather than replacing them, allowing clinicians to use lower doses of these medications and thereby often avoiding side effects of higher doses.

The presence of hypertension, electrolyte (e.g., K and Mg) abnormalities and heart failure should be considered when selecting the most appropriate agent. There are a number of drugs that have been tried; however, this article will be restricted to medications that should be considered by generalist physicians who are not operating in a specialist clinic dedicated to hypertension/OH. Within this scope there are two commonly used drugs – fludrocortisone and midodrine.

6. Fludrocortisone

Fludrocortisone (florinef) is an oral synthetic mineralocorticoid analog that sensitizes peripheral alpha receptors and expands intravascular volume by increasing renal sodium reabsorption. Consequently fludrocortisone is contraindicated in fluid overload conditions (CHF, ascites, etc.). It also has a pressor effect that treats OH by increasing peripheral vascular resistance.[17] It is usually the first choice for most patients with OH. The starting dose is 0.1 mg daily and this should be supplemented with a diet adequate in fluids and in sodium. Dose increments should be no more than 0.1 mg per day every 1-2 weeks if patients tolerate it without side effects. Patients are monitored with serial postural blood pressure readings taken at different times of the day including morning, afternoon and before bed[18], although this can be challenging in the outpatient setting. Outpatients are advised to keep a log of supine vs. standing blood pressure readings for at least 1-2 weeks. The effect of this medication is only transient; its long-term benefits may be related to potentiation of the pressor effect of norepinephrine and angiotensin II.[13,19]

Common side effects are supine hypertension, edema, headaches, heart failure, hypokalemia and hypomagnesimia. Consequently patients need to be monitored for new onset edema and for heart failure; some clinicians will not prescribe this medication without a cardiac echocardiogram, although that practice is not evidence based. Potassium and magnesium levels should be monitored periodically. Above 0.3 mg patients may experience corticosteroid side effects. For a more detailed list of side effects click here.

7. Midodrine

Midodrine is a short-acting pressor that can be used if patients do not already have supine hypertension. Midodrine has alpha 1 adrenergic activity; it does not cross the blood brain barrier and its pressor effect is due to both arterial and venous constriction.[20] This drug significantly increases one-minute standing systolic BP compared with placebo and improves clinical symptoms of OH including dizziness, lightheadedness and syncope.[21,22] Many nephrologists use this after hemodialysis for patients who experience OH in the immediate post-dialysis period.

Dosing starts at 2.5 mg and can be titrated up slowly to 10 mg three times a day while monitoring for supine hypertension (often the limiting factor in the use of this medication). The medication should not be used in patients with uncontrolled hypertension. Other examples where midodrine is not the drug of choice is in patients with severe heart disease, urinary retention and underlying supine hypertension. Some clinicians employ the medication in patients with mild supine hypertension by giving the medication at bedtime and raising the head of the bed 10-20 degrees.[23] This practice carries some risk and is employed at the discretion of the treating physician.

For other potential side effects of midodrine click here. Patients who are started on midodrine are instructed to take their postural blood pressures over several days at least three times daily, as with florinef. If they note a significant rise in BP they should contact their physician immediately.

In some cases a combination of florinef and midodrine can be effective. Some clinicians employ combinations of low doses of both medications to avoid the side effects of higher doses.

If a combination of non-pharmacological and pharmacological (fludrocortisone and/or midodrine) therapies is not effective and it is judged that the patient remains at significant risk of falls and trauma due to OH then referral to a specialist should be considered. Other medications have been studied but the studies have been small and full efficacy remains less clear. Such medications are outside the scope of this general article and are best left to specialists in hypertension and OH. For those interested in reading more regarding such specialized treatments we recommend the 2012 systematic review by Logan,[6] as well as the American Society of Hypertension Position Paper: Evaluation and Treatment of Orthostatic Hypotension.

Who, when and where to refer a patient with OH for evaluation

Some patients may require referral to specialized autonomic dysfunction services or hypertension specialists. Where these services are not available or where front-line clinicians need help in employing the non-pharmacological management strategies (which often require a multidisciplinary team) and/or florinef and midodrine, a referral to local specialists in geriatric medicine or care of the elderly is also appropriate.

Conclusion

In the case presented in the beginning of this article, we identified that it was important to highlight possible medications that could be contributing to Mr. B.'s symptoms and follow a systematic approach in managing his symptoms and preventing further postural drops. His weight loss might be a side-effect of his cholinesterase inhibitor. We encouraged increased oral intake and prescribed a supplement. Oral intake improved. We initiated non-pharmacological interventions including educating him and his family regarding triggers of OH and provided instructions to get up slowly from the bed, to place his bed in the reverse Trendelendurg position (with resources) and to increase fluid intake during the day. This resulted in minimal improvement. Given that his echocardiogram showed an EF of 32 percent we avoided fludrocortisone. He was started on midodrine and eventually his dose was titrated to 2.5 mg three times a day (in addition to continuing non-pharmacological approaches) with good effect. It is possible that the non-pharmacological efforts decreased the overall midodrine dose requirement which, in turn, helped avoid higher doses that might have resulted in supine hypertension.

For more resources on OH see www.posturalhypotension.ca.

Figure 1.

Figure 2. www.bramptonfootclinic.com

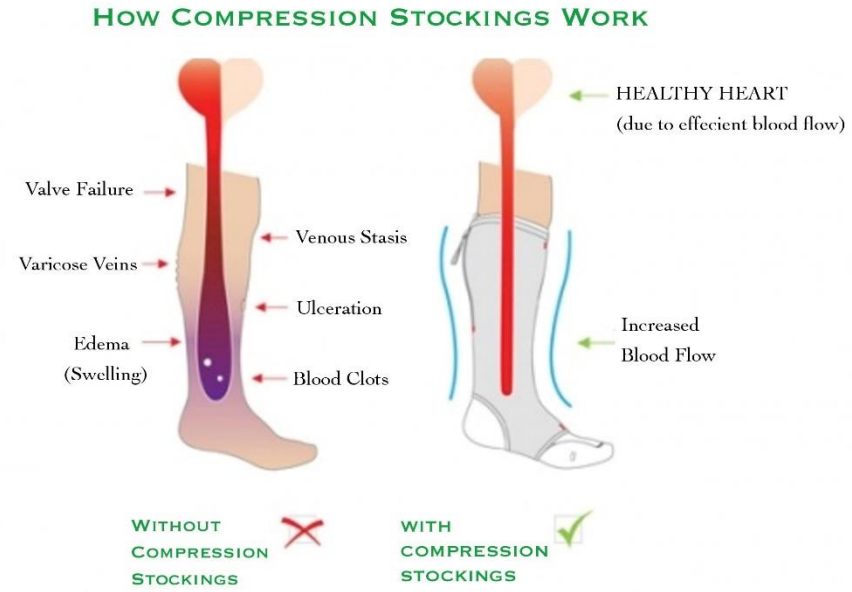

Figure 3.

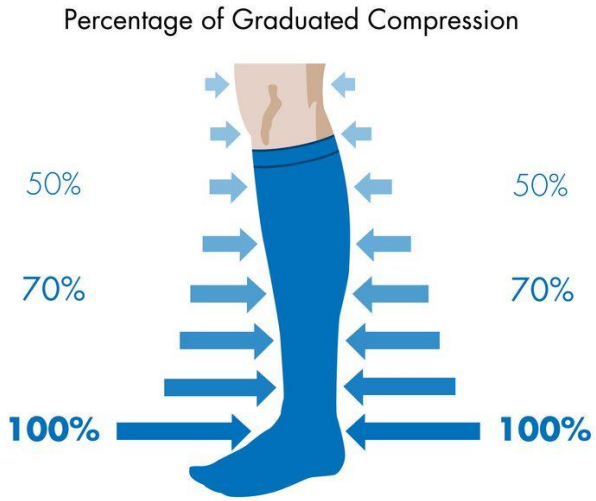

Table 1. DDX of postural hypotension – 4D-AID acronym

1. Causes associated with a compensatory tachycardia – 4Ds

a. Deconditioning
b. Dysfunctional heart
   - Myocardium (very low left ventricular ejection fraction)
   - Aortic stenosis
c. Dehydration
   - Disease (e.g., acute illness, adrenal insufficiency)
   - Dialysis (post-dialysis dry weight too low)
   - Drugs
     - Diuretics
     - Anorexic drugs – narcotics, digoxin, antibiotics, cholinesterase inhibitors
d. Drugs – 6 ANTIs
   - Anti-hypertensives
   - Anti-anginals
   - Anti-parkinsonian medications (e.g., levodopa)
   - Antidepressants (e.g., anti-cholinergic tricyclics)
   - Anti-psychotics (anti-cholinergic effect)
   - Anti-BPH (e.g., terazosin, tamsulosin)

2. Causes that present with *lack* of compensatory tachycardia – AID

e. Autonomic dysfunction
   - Diabetic autonomic neuropathy (consider if patient has peripheral neuropathy)
   - Low B12
   - Hypothyroidism
   - ETOH abuse
   - Parkinsonism (Parkinson's disease, progressive supranuclear palsy, multisystem atrophy; e.g., Shy-Drager syndrome)
   - Amyloid
f. Idiopathic (Bradbury-Eggleston)
   - Depletion of norepinephrine from sympathetic nerve terminals
g. Drugs
   - Beta-blockers

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