Treatment of Orthostatic Hypotension: Preserving Function and Quality of Life

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This article focuses on the treatment of orthostatic hypotension (OH) in the elderly. OH is a common problem that can affect an elderly person’s function and quality of life. A careful history and physical examination must be done to make an accurate diagnosis and to determine the causes of OH. Treatment should focus on the causes of OH. Both nonpharmacological and pharmacological interventions are reviewed.

Key words: orthostatic hypotension, fludrocortisone, midodrine, octreotide, erythropoietin.

In response to the confusion surrounding the existence of multiple definitions of orthostatic hypotension (OH), a consensus statement has been developed to standardize the meaning of this medical condition. OH is defined as a reduction of systolic blood pressure (BP) of at least 20 mmHg, or a reduction of diastolic BP of at least 10 mmHg, within three minutes of standing.1

The prevalence of OH in the elderly ranges from 5–33%.2-4 This variability may be the result of different definitions used and the range of populations considered, from frail older nursing home patients to healthy older people living in the community. The prevalence of OH can be as high as 50% in frail older nursing home patients.2

Normal Orthostatic Blood Pressure Regulation

Blood pools in the lower extremities when a person stands up. This results in a decrease in venous return, which reduces stroke volume and cardiac output. The body responds to the decreased cardiac output by stimulating the baroreceptors, which stimulate sympathetic outflow and inhibit parasympathetic outflow. This increases the heart rate and causes vasoconstriction of the vessels. The latter increases peripheral vascular resistance (PVR). Both these measures maintain the systemic BP.5

The Elderly and Orthostatic Hypotension

In the elderly, an acute heart rate increase in response to acute orthostatic stress is much smaller and takes longer to achieve. The blunted heart rate response has been attributed to diminished baroreceptor sensitivity.5 However, OH is not caused by age alone. Rather, OH is more common in the elderly because, in addition to normal age-related changes, they are more likely to have chronic diseases and take medications that can cause OH.

Causes of Orthostatic Hypotension

OH is not a diagnosis but rather a clinical finding. There are many causes for it, which can be divided into autonomic and non-autonomic causes (Table 1).6 Non-autonomic causes are much more common in the elderly and include volume contraction, medications and immobility. Volume contraction can be caused by inadequate intake of fluids, fluid loss, diarrhea, diuretics and diabetes insipidus. An uncommon but important cause of OH is adrenal insufficiency.

Several classes of medications are thought to cause OH (Table 1). Although medications may cause OH, medications should be used when they are clinically indicated as the benefit usually outweighs the risk of causing OH. One interesting reason for treating hypertension is that it may improve postural BP regulation. It is known that hypertension decreases baroreceptor sensitivity.5 A National Health study of BP measured in the supine and sitting positions and involving over 8,000 survey participants suggested that the increase in OH with age may be due to an age-associated increase in supine systolic BP, rather than age alone.7

There are many autonomic disorders that cause OH. These can be divided into primary and secondary causes (Table 1). Primary causes of autonomic failure are uncommon but very difficult to treat. Secondary causes of autonomic disorders can be divided further into central, spinal and peripheral.

Post-prandial hypotension is thought to be caused by a peripheral autonomic disorder. It is defined as a decrease in systolic BP of 20 mmHg or more after a meal. It is thought to be distinct from OH but can occur in conjunction with it. The mechanism of post-prandial hypotension is not completely understood.8

Clinical Evaluation

OH can be asymptomatic or symptomatic. Symptoms caused by OH may include lightheadedness, dizziness, blurred vision, weakness, fatigue, cognitive impairment, nausea, palpitations, tremulousness, headache and neck pain.1 A careful history and physical examination are important for the diagnosis and management of OH. Evidence of autonomic dysfunction should be sought. OH should also be considered when falls and syncope have occurred. OH can occur intermittently in patients depending on the time of day and medication use.2 OH is more prevalent first thing in the morning and repeated BP measurements are often required to make a diagnosis.

It is recommended that the patient be supine for at least five minutes before having their BP and heart rate taken. This ensures a stable situation when the supine BP is taken. The patients should then have their BP and heart rate measured when they first stand up. In autonomic dys-
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function, the HR does not increase when the patient changes from a supine to standing position. Although there is some debate on when repeat measurements should be done, it is reasonable to do repeat measurements at one and three minutes. It should be noted that BP taken when the patient sits and then stands could result in a missed diagnosis of OH.

Treatment

Treatment of OH should focus on its causes, with action taken to correct any reversible factors. Medications that can cause OH should be analysed for their clinical benefit. The use of unnecessary drugs should be discontinued. Necessary drugs should have their doses decreased or their dosage interval increased. If the OH persists after reversible causes have been addressed, then both nonpharmacological and pharmacological treatments should be considered (Table 2). Treatment should not focus on achieving a target standing BP, but should aim to preserve function and enhance quality of life with minimal side effects. Treatment may not completely prevent OH but it can improve a patient’s function.

Nonpharmacological Treatments

Patients need to be educated about factors that contribute to OH so that their effects can be avoided or minimized (Table 2). They should be advised to change their positions slowly to give their body time to adapt to the change. They should be particularly careful in the morning and after meals. Patients should avoid becoming dehydrated. Alcohol and hot environments should also be avoided as they can result in vasodilatation.

A liberal salt intake should be encouraged unless there are clinical contraindications, which is unusual. As meals can cause post-prandial OH, smaller and more frequent meals are advised with the biggest meal being served in the evening. Caffeine can help limit OH as it has pressor effects. Patients can be advised to drink two cups of coffee (240mg of caffeine) with breakfast and lunch. However, patients can develop a tolerance to caffeine.

Exercise can lower BP through skeletal muscle vasodilatation that is not opposed by sympathetic vasoconstriction. Regular exercise, however, is important for health, and prolonged recumbency makes OH worse. Exercising in a horizontal position, such as during swimming, can be beneficial. Overall, it is important for patients to exercise but they should be warned that certain types of exercise could worsen OH.

The head of a patient’s bed should be elevated to 30 degrees by using wooden blocks. This is thought to reduce OH by activating the renin-angiotensin-aldosterone system, and through other mechanisms that reduce recumbency-induced diuresis.

In a study with a small number of patients, leg-crossing and squatting improved orthostatic tolerance by increasing BP in patients with autonomic dysfunction. Compression stockings that go to the waist can be tried, although they can be difficult to get on and off and are uncomfortable, especially in hot conditions.

Table 1

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<td><strong>Non-autonomic Causes</strong></td>
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weather. They are also contraindicated in patients with significant skin ulcers.

Pharmacological Treatments

Many drugs have been tried to treat OH. Two commonly used drugs are fludrocortisone and midodrine. Fludrocortisone is a synthetic mineralocorticoid that increases BP by causing sodium retention, which occurs over several days. The full effect of the drug is therefore seen over a period of one to two weeks. Patients also need to gain 5–8 pounds in order for fludrocortisone to have an optimal effect. The usual starting dose is 0.1mg per day orally. The dose should be altered weekly or biweekly by increments of 0.1mg, and few patients require more than 0.4mg per day. Corticotropin (ACTH) suppression can be seen at doses of 2mg per day. Headache is a common side effect, especially in people younger than 50 years. Fludrocortisone can interact with warfarin so some patients may require their warfarin dose to be increased.

A prospective case series evaluated the tolerance of fludrocortisone in older patients with hypotensive disorders. Sixty-four consecutive patients who were older than 65 years of age (mean age 80 years) and had one or more hypotensive disorders were followed. Hypotensive disorders were classified as OH, vasodepressor carotid sinus syncope and/or vasodepressor neurocardiogenic syncope. OH occurred by itself or in combination in 64% of the patients. Doses of 0.05–0.1mg per day were used except in one patient who received 0.2mg per day. The mean duration of treatment was one year, during which 13 patients died of unrelated causes. In the remaining patients, 33% discontinued fludrocortisone at a mean of five months. Reasons for discontinuing treatment were hypertension, cardiac failure, depression, edema and unspecified. Hypokalemia developed in 24% of patients at a mean of eight months. The authors concluded that fludrocortisone, even in low doses, was poorly tolerated in older patients with hypotensive disorders.

Midodrine is a prodrug that is metabolized to desglymidodrine after absorption. It is a selective α1-adrenoceptor agonist, and is thought to work by constricting arterioles and veins. The usual starting dose is 2.5mg at breakfast and lunch, which can be increased by 2.5mg increments daily until there is an effective response, or up to a maximum of 30mg per day. Most patients require three times a day dosing. It is contraindicated in patients with severe heart disease, acute renal disease or urinary retention.

Two randomized, double-blinded, placebo controlled studies involving a total of 268 patients evaluated the efficacy and safety of midodrine in neurogenic

An Illustrated Definition of Orthostatic Hypotension

Blood Pressure measured while lying down for at least five minutes:
Systolic: 164 mmHg
Diastolic: 70 mmHg

Blood Pressure measured while standing:
Systolic: 130 mmHg
Diastolic: 60 mmHg

Orthostatic hypotension is defined as a reduction of systolic blood pressure of at least 20 mmHg, or a reduction of diastolic blood pressure of at least 10 mmHg, within three minutes of assuming an upright posture from a supine position.

Upon standing, venous pooling in the lower limbs contributes to a fall in arterial blood pressure. The elderly have more problems adjusting to this orthostatic stress, and are therefore more vulnerable to orthostatic hypotension.
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OH. In the five-week study involving 97 patients, age ranged from 22–86 years (mean age 61 years). In the six-week study involving 171 patients, the mean age of the treatment and placebo groups were 60 and 59 years, respectively. Concomitant treatment with fludrocortisone, high salt diet and compression garments were allowed, but no changes to concomitant treatments were allowed during the study.

These studies showed that midodrine in doses of 10mg p.o. t.i.d. significantly improved standing BP and clinical symptoms of OH. In the five-week study, the clinical symptoms that improved were syncope, dizziness/lightheadedness, low energy, weakness/fatigue, impaired ability to stand and feelings of depression. In the six-week study, there were improvements in symptoms of lightheadedness and an improved global symptom relief score. The global symptom relief score was defined as a composite improvement in orthostatic tolerance manifested as symptoms of lightheadedness and improvement in the patients’ ability to remain on their feet and perform orthostatic activities of daily living.

In the five-week study, scalp pruritus/tingling was the most frequent side effect with midodrine treatment, occurring in 13.5% of patients. The other most commonly reported side effects were supine hypertension (8%), urinary urgency (4%) and headache (3%). In the six-week study, the most frequent side effects were piloerection (13%), scalp or general pruritus (10% and 2%, respectively), scalp or general paresthesia (9% each), urinary retention (6%), supine hypertension (6%) and chills (5%). Supine hypertension can be reduced when the last daily dose of midodrine is given four hours before bedtime.

Octreotide and recombinant erythropoietin have been used in specific circumstances. Octreotide is a somatostatin analogue and is beneficial in post-prandial hypotension. It inhibits the release of gastrointestinal peptides that have vasodilatory properties. Doses of 25–50µg subcutaneously half an hour before a meal can reduce post-prandial hypotension. Nausea and abdominal colic may result. It has also been used in combination with midodrine and has a synergistic effect on improving OH. Recombinant erythropoietin has been tried in patients with anemia and autonomic dysfunction. It has been used in doses of 25–75U/kg three times a week. In addition to increasing the red blood cell count, the BP often rises about 10 mmHg. The mechanism by which this happens is not completely understood. Both treatments have been studied in a small number of patients and are expensive.

Other treatments for OH have included ephedrine, yohimbine, clonidine, pindolol, hydralazine, desmopressin, metoclopramide, indomethacin and ergot alkaloids. These drugs were minimally effective and were often intolerable due to side effects. In severe cases of refractory OH from autonomic failure which caused patients to be bedridden, ambulatory norepinephrine infusion was able to improve OH enough that they could be mobilized.

Summary

The majority of elderly patients with OH will respond to conservative measures. Reversible causes should be looked for and modified. Nonpharmacologic measures should be tried next. Most clinicians will start with fludrocortisone and will add midodrine if additional treatment is necessary. Supine hypertension is an important side effect that often limits effective therapy. Combination therapy can be effective and may reduce side effects by allowing the combined dosages of the medications to be reduced. Patients with primary autonomic failure causing OH are more difficult to treat. The goal of therapy is to improve function and quality of life with minimal side effects.

No competing financial interests declared.

References

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