CLINICAL VIGNETTE

Recurrent Falls due to Orthostasis, Overview of Management

Shelley Schwartz, MD, MBA and Rahul Vasavada, MD

Introduction

Orthostatic hypotension is defined by a drop in systolic blood pressure of at least 20 mmHg or diastolic blood pressure of at least 10 mmHg after a change to an upright position. The incidence of orthostatic hypotension increases with age and is most prevalent in patients over the age of 65. It has been reported in over 20% of 65+ year old patients, especially in those hospitalized.[1] With the prevalence of orthostatic hypotension in hospitalized patients, it is important to develop algorithms to treat and prevent recurrence.

Case Report

A 79-year-old male with Parkinson's disease complicated by autonomic dysfunction and orthostatic hypotension presented with recurrent falls with multiple kyphotic fractures. He reported recent numerous falls that were preceded by a prodrome of dizziness. He also noted decrease of appetite with weight loss. The patient and spouse reported recent worsening of low blood pressure readings. These were likely due to a combination of progression of autonomic dysfunction and poor fluid intake. He was recently seen by his neurologist who recommended further rehabilitation and initiation of midodrine. However, he was not compliant with midodrine, though he was compliant to carbidopa-levodopa. He had another episode of orthostatic hypotension at home with a brief loss of consciousness. He fell, hitting his head and right shoulder. He presented to the emergency department where imaging showed right comminuted and displaced proximal humerus fracture and right lateral 4th/5th rib fractures. Initial syncope evaluation and brain imaging were negative.

Orthopedic surgery was consulted and the patient underwent successful right reverse shoulder arthroplasty. His hospital course was complicated by episodes of delirium which were managed conservatively. Post-operatively he continued to have significant orthostatic hypotension with systolic blood pressure as low as 70 mmHg. Midodrine was increased to 10 mg three times daily, and he was started on T.I.D daily salt tablets in addition to TED hose and an abdominal binder. He was on a regular diet with encouragement of fluid/oral intake. Physical therapy sessions allowed sitting and standing without syncope or pre-syncope by day of discharge. He was transferred to an Acute Rehabilitation Unit (ARU) for continued physical and occupational therapy.

At ARU he continued to have episodes of orthostatic hypotension. The family was advised to help the patient to a supine position when he developed orthostatic symptoms. Salt tablets, TED hose and abdominal binder were continued and increased fluid intake encouraged. Medications were again reviewed, and he was not taking any medications causing ortheostasis. Midodrine was increased to 15 mg three times daily, and he was also started on droxidopa 100 mg three times daily. He experienced fewer episodes of orthostatic hypotension during his rehabilitation course, although intermittent orthostatic events still continue.

Discussion

Orthostatic hypotension occurs when autonomic reflexes are impaired or intravascular volume is depleted. The formal definition of orthostatic hypotension is a sustained reduction of systolic blood pressure of at least 20 mmHg or diastolic blood pressure of 10 mmHg within three minutes of taking an upright position.[2] Standing normally results in a pooling of blood in the lower extremities, which triggers a number of compensatory responses which lead to a small fall in systolic blood pressure, an increase in diastolic blood pressure and possible increase in heart rate. In patients with orthostatic hypotension, one or more of these compensatory mechanisms fail.[3] This can result in a symptomatic or asymptomatic reduction in blood pressure. Clinical presentations are varied and range from cognitive slowing with hypotensive unawareness or unexplained falls to classic pre-syncope (dizziness, lightheadedness) and syncope.[3,4] This can be a significant clinical problem.

Many disorders can cause orthostatic hypotension. The major mechanisms are baroreflex dysfunction, severe volume depletion, adverse effects of medications, and chronic hypertension. Common medications that can induce orthostatic hypotension include alpha-1 blockers (such as terazosin or tamsulosin), selective serotonin reuptake inhibitors (SSRIs), antihypertensives and second-generation antipsychotics. Additionally, neuropathies associated with diabetes mellitus, vitamin B12 deficiency or others can result in autonomic dysfunction and orthostasis. A large portion of orthostatic hypotension patients are due to underlying neurodegenerative disorders causing autonomic failure. One study reported 27% of orthostasis cases were due to underlying neurodegenerative conditions. These included Parkinson’s disease, Lewy Body Dementia, and

Multiple system atrophy.[3] This phenomenon is known as Neurogenic Orthostatic Hypotension (NOH).[5]

In our patient, Parkinson's disease was the cause of NOH due to autonomic failure. The goal in these patients is to decrease falls and symptom burden rather than to achieve a specific blood pressure target. Initial treatment starts with non-pharmacologic measures, which may provide effective symptom relief while avoiding adverse effects associated with adding new medications. Measures include increasing salt and water intake, lifestyle modification, dietary interventions, the use of compression stockings and abdominal binders, and the removal of potential offending medications.[6,7] Specific lifestyle modifications include standing up slowly, avoidance of heat exposure, marching in place prior to standing, voiding in a seated position, counter-pressure maneuvers such as crossing legs or clenching fists, and sleeping with the head of bed elevated. These measures are the foundation of conservative management of NOH. Additionally, increasing water intake to about 2 liters per day has been shown to help with NOH. If these measures are insufficient to prevent symptoms and complications of NOH, then pharmacotherapy may be needed.

Patients with persistent symptoms that impact daily function despite non-pharmacologic interventions, meet indications for pharmacotherapy. There are two main approaches to pharmacologic treatment: volume expansion and increasing vascular tone through sympathomimetic agents. The mineralocorticoid agent, fludrocortisone can be used to expand extracellular fluid volume, but is often associated with supine hypertension and should be used with caution in patients at risk for fluid overload, including heart failure. Pharmacologic agents have limited data with a low certainty of efficacy for NOH. Two drugs are approved by the US Food and Drug Administration (FDA) for the treatment of symptomatic NOH: midodrine, an alpha-adrenergic agonist, and droxidopa, a norepinephrine precursor.[7] Midodrine has valuable efficacy and should be started at 2.5 mg. Side effects include supine hypertension and urinary retention. Midodrine's half-life is approximately 40 minutes. Droxidopa is started at a 100 mg and can be increased slowly. It can be given when patients are more active. Droxidopa can be less effective for patients receiving high dose carbidopa because the conversion of droxidopa to norepinephrine may be blocked. For patients with suboptimal response to monotherapy, multiple medications can be added for synergistic benefit.

Conclusion

Despite non-pharmacologic and pharmacologic treatment strategies, the symptomatic burden of NOH remains high in patients with Parkinson's disease. Blood pressure fluctuations may remain a management challenge. Neurogenic Orthostatic Hypotension patients need for further therapeutic and safety studies.

REFERENCES

1. **Saedon NI, Pin Tan M, Frith J**. The Prevalence of Orthostatic Hypotension: A Systematic Review and Meta-Analysis. *J Gerontol A Biol Sci Med Sci*. 2020 Jan 1;75(1):117-122. doi: 10.1093/gerona/gly188. PMID: 30169579; PMCID: PMC6909901.
2. **Freeman R, Wieling W, Axelrod FB, Benditt DG, Benarroch E, Biaggioni I, Cheshire WP, Chelimsky T, Cortelli P, Gibbons CH, Goldstein DS, Hainsworth R, Hilz MJ, Jacob G, Kaufmann H, Jordan J, Lipsitz LA, Levine BD, Low PA, Mathias C, Raj SR, Robertson D, Sandroni P, Schatz IJ, Schondorf R, Stewart JM, van Dijk JG**. Consensus statement on the definition of orthostatic hypotension, neurally mediated syncope and the postural tachycardia syndrome. *Auton Neurosci*. 2011 Apr 26;161(1-2):46-8. doi: 10.1016/j.autneu.2011.02.004. Epub 2011 Mar 9. PMID: 21393070.
3. **Robertson D, Robertson RM**. Causes of chronic orthostatic hypotension. *Arch Intern Med*. 1994 Jul 25;154(14):1620-4. PMID: 8031210.
4. **Mol A, Bui Hoang PTS, Sharmin S, Reijnierse EM, van Wezel RJA, Meskers CGM, Maier AB**. Orthostatic Hypotension and Falls in Older Adults: A Systematic Review and Meta-analysis. *J Am Med Dir Assoc*. 2019 May;20(5):589-597.e5. doi: 10.1016/j.jamda.2018.11.003. Epub 2018 Dec 21. PMID: 30583909.
5. **Baschieri F, Sambati L, Guaraldi P, Barletta G, Cortelli P, Calandra-Buonaura G**. Neurogenic orthostatic hypotension in early stage Parkinson's disease: New insights from the first 105 patients of the BoProPark study. *Parkinsonism Relat Disord*. 2021 Dec;93:12-18. doi: 10.1016/j.parkreldis.2021.11.002. Epub 2021 Nov 4. PMID: 34758441.
6. **Mills PB, Fung CK, Travlos A, Krassioukov A**. Nonpharmacologic management of orthostatic hypotension: a systematic review. *Arch Phys Med Rehabil*. 2015 Feb;96(2):366-375.e6. doi: 10.1016/j.apmr.2014.09.028. Epub 2014 Oct 14. PMID: 25449193.
7. **Wieling W, Kaufmann H, Claydon VE, van Wijnen VK, Harms MPM, Juraschek SP, Thijs RD**. Diagnosis and treatment of orthostatic hypotension. *Lancet Neurol*. 2022 Aug;21(8):735-746. doi: 10.1016/S1474-4422(22)00169-7. PMID: 35841911; PMCID: PMC10024337.