ORTHOSTATIC HYPOTENSION (OH): CONSIDERATIONS FOR MANAGEMENT

WHAT IS THE PREVALENCE OF ORTHOSTATIC HYPOTENSION (OH)?

- The prevalence of OH varies depending on the age and comorbidities of the population. The prevalence of OH can range from ~16-20% in community residents & as high as ~50% in nursing homes, and increases exponentially with age. It is of importance due to its association with falls, fractures, transient ischemic attacks, syncope and myocardial infarction, which all can cause serious morbidity and mortality risk.

WHAT IS ORTHOSTATIC HYPOTENSION?

- A sustained ↓ in systolic BP ≥20mmHg or in diastolic BP ≥10 mmHg within 3 minutes of standing from sitting or supine position.
- May be symptomatic, asymptomatic or atypical.
- Common symptoms: dizziness, light-headedness, blurred vision, fatigue, nausea, palpitations, and headache.

WHAT ARE THE CAUSES OF ORTHOSTATIC HYPOTENSION? 7,11,12

Table 1: Causes of OH [may commonly be multifactorial, especially in older or if medically complex]

<table>
<thead>
<tr>
<th>4Ds:</th>
<th>Deconditioning, Dysfunctional Heart Rate, Dehydration, Drugs &amp; Drugs</th>
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<tbody>
<tr>
<td>Acute/ reversible</td>
<td>Dehydration, medications (see Table 3), deconditioning, fever</td>
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<tr>
<td>Chronic/non-reversible</td>
<td>Cardiac failure, diabetes mellitus, Parkinsonism, multiple system atrophy, trauma (blunt to chest)</td>
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<tr>
<td>Non-neurogenic OH</td>
<td>Cardiovascular: MI, aortic stenosis, constrictive pericarditis, advanced cardiac failure, hypertrophic obstructive cardiomyopathy (HOCM), arrhythmias, large varicose veins</td>
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<tr>
<td>Endocrine</td>
<td>Endocrine and renal: adrenal insufficiency, diabetes insipidus, hypoadosteronism, renal concentrating defect</td>
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<tr>
<td>Neurogenic</td>
<td>Venous: alcohol, postprandial dilation (splenic blood vessels), hot environment, prolonged standing</td>
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<tr>
<td>Primary causes</td>
<td>Reduced intravascular volume: hemorrhage, burns, salt-losing nephropathy</td>
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<tr>
<td>Secondary causes</td>
<td>Autoimmune &amp; inflammatory: all-cause inflammation, fibromyalgia, chronic fatigue, headache, neuropathy</td>
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MANAGEMENT OVERVIEW

- Assess Acute Medical Issues, Medications, & Hydration Status 7,11,14
- Assess for Drug Induced Causes Of OH (see Table 3)
- → α-blockers e.g. terazosin; antihypertensives: e.g. diuretics (preferred alternatives: ACEI/ARB, or adjust or split dose); antiparkinson’s, antipsychotics, barbiturates, ethanol, insulin, MAOIs monamine oxidase inhibitors, nitrates, opiates, phosphodiesterase inhibitors, sedatives, TCAs (alternative: SSRI), & trazodone
- Consider stopping, reducing or changing the offending drug/dose
- Get Up Gradually: avoid getting up or moving too quickly (e.g. count to 15 before upright activities)
- Stay Cool: avoid exposure to hot environments (e.g. hot showers)
- Fluid (1.5-3L daily) or salt intake (up to 2.3-4.6 g NaCl daily in food or as 1g tablets) unless contraindicated (e.g. heart failure, hypotension).
- Drink ~500mL of water as bolus, ↑ BP in 5-30+ minutes
- Syncope Avoidance Maneuvers: leg crossing, bending forward, squatting, toe raise, limb & abdominal contraction; give yourself a hug while standing.
- Eat small, frequent low carbohydrate meals (e.g. 6 small meals vs. 3 large meals) to prevent postprandial worsening of OH.
- ↑ caffeine intake: 1-2 cups of coffee/tea with meals if postprandial OH may be used in addition to nonpharmacological therapies, especially in NOH.
- Note: [Meds treating OH can also cause supine HTN]

e) PHARMACOLOGIC MANAGEMENT OPTIONS 1,2,3,7,10,11,12,14,15,17,19

When non-pharmacological measures are inadequate, pharmacologic agents may be used in addition to nonpharmacological therapies, especially in NOH.

Table 2: Select Drugs For Treatment Of Orthostatic Hypotension

<table>
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<tr>
<th>DRUG</th>
<th>DOSE/ MOA/ PHARMACOKINETICS</th>
<th>ADVANTAGES/ DISADVANTAGES</th>
<th>CONTRAINDICATIONS (CI)/ ADVERSE EFFECTS (AE)/ DRUG INTERACTIONS (DI)/ MONITOR (M)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fludrocortisone FLORINEF</td>
<td>0.1mg tablets</td>
<td>0.1 to 0.3mg daily. ↑ dose weekly or until pedal edema (if start low: 0.05mg) Maximum: 1mg/ day</td>
<td>Synthetic mineralocorticoid (sodium &amp; water retention) Adv: Considered first line therapy after failure of non-pharmacological measures Dose limiting AE. K’s supplementation usually required. Fluid overload</td>
</tr>
<tr>
<td>Midozoline AMATINE, g 2.5, 5mg tablets</td>
<td>2.5mg TID, ↑ 2.5mg weekly until max dosage (for best results, AM dose given early and PM dose no later than 6pm) Maximum: 10mg TID MOA: α-1-agonist</td>
<td>Can be used with fludrocortisone in refractory individuals PRN scheduling, taken 30 to 45 minutes before upright activities ↑ DI: Caution elderly taking meds that may cause orthostatic hypotension, sitting to urinate may be preferred.</td>
<td>CI: CAD, HF, acute renal failure, severe heart disease, pulmonary edema, thyrotoxicosis, thyrotoxic myopathy AE: supine HTN, piloerection, pruritus, paraesthesia M: may ↑ antidiuretic hormones (e.g. aldosterone), BCG, corticosteroid effect, ↑ AE of natalizumab, taper off steroids prior to starting natalizumab</td>
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Other Considerations:

- Antihypertensives should be discontinued at all the same time in people with OH. A stepwise approach should be considered if discontinuing and tapering these medications. While the risk of falls is ~2.5 times higher in the elderly with uncontrolled HTN, some relaxation of the BP goals may have to occur in order to manage the OH symptoms. Often stopping antihypertensives can treat OH in more than half of people with these symptoms.
- Pacemaker therapy: Atrial tachypacing option for OH and bradycardia. Dual chamber pacemakers can treat severe OH.
When possible, stop the medication of concern or reduce the dose of the medication before switching to another agent. Control of OH may require decrease or change to tamulosin or alfuzosin (if for BPH). If an individual cannot stop an antihypertensive, it may be replaced by agents that are less likely to cause OH. Although for some, non-pharmacologic measures with appropriate antihypertensive medications may be sufficient.

**Table 3: Medications That May Worsen OH and Possible Alternatives**

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<thead>
<tr>
<th>Medications That May Worsen OH</th>
<th>Alternatives (less likely to cause OH)</th>
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<tbody>
<tr>
<td>CV 8 blockers (e.g. propranolol &gt; metoprolol) α agonists (e.g. clonidine, methyldopa) Diuretics (e.g. furosemide &gt; hydrochlorothiazide, chlorthalidone) α blockers (e.g. doxazosin, prazosin, terazosin) Non-DHP CCB (e.g. verapamil, diltiazem) CNS TCA’s (e.g. amitriptyline &gt; nortriptyline; clomipramine, doxepin &gt;6mg/day, imipramine, trimipramine)</td>
<td>change to an ACEI or an ARB consider timing options. May split dose of antihypertensives e.g. ACEI or ARB, or nighttime dosing of at least one antihypertensive change to tamulosin or alfuzosin (if for BPH) DHP CCB (e.g. amlodipine, felodipine; Avoid nifedipine IR (Beers criteria) considering giving at nighttime ≤ SSRI or SNRI (if treating depression or anxiety) or mirtazapine if TCA indicated, may consider nortriptyline</td>
</tr>
</tbody>
</table>

Consider a step-wise approach by tapering/discontinuing one antihypertensive at a time. If using both a BB & clonidine, taper BB first, several days before tapering clonidine to risk of rebound HTN.

**SUMMARY: HOW SHOULD ORTHOSTATIC HYPOTENSION BE MANAGED?**

A medication assessment should be done to determine if any medications may be contributory. When suitable, consider a trial of stopping or reducing medication(s) of concern or switching to another agent. In [comorbidities] such as HF, reducing doses or stopping medications could mean sacrificing life-saving effects of drugs such as ACEI & β-blockers; facilitate risk vs benefit discussions with patient/care-giver to allow for informed decisions. Non-pharmacological measures are important in management of OH and can be used while medications are being changed or adjusted and after the change if symptoms are still present. If OH symptoms continue to remain problematic, drug therapy may be added to non-drug measures to manage OH. [Most OH related drug trials were studied in nO]H.] Assessment of fluid status and management of dehydratio is important.

**New Drug (USA): DROXIDOPA**

L-Dihydroxyphenylserine, 100, 200, 300 mg caps po TID; FDA Approval Feb/14 for Treatment of symptomatic NOH. Shown success in patients with autonomic failure and in dopamine B hydroyxylase deficiency but not been studied in elderly/complex medical patients. Effectiveness beyond 2 weeks not demonstrated. Caution: FDA Black Box: may cause supine hypertension. AE: nausea, headache, dizziness. Hypertension. (Rare: possible neuroleptic malignant syndrome, & may exacerbate heart disease or stroke).

**References:**


**For more information on our RxFiles Academic Detailing service in SK, or one of our books, go to www.RxFiles.ca!!!**

Pictured at left:

1) RxFiles Drug Comparison Charts 10th Ed.

2) Geri-RxFiles – Assessing Medications in Older Adults
Additional references:

Notes:
- Suggest measure BP at 1 minute and 3 minutes after standing.
    [http://jamanetwork.com/journals/jamainternalmedicine/fullarticle/2645147](http://jamanetwork.com/journals/jamainternalmedicine/fullarticle/2645147)