Non-Drug Treatment for Orthostatic Hypotension

Generally it is best to start with non-pharmacological treatment, and proceed to drug treatment only when this fails. Note that measures such as voloume expansion with increased salt and fluid, moderate exercise and tilt training are relatively safe but their effectiveness has not been demonstrated by controlled trials (Kapoor, 2003). Nevertheless, we think it is reasonable to give these things a try.

1. Use an automatic blood pressure cuff (about $30 at Walgreens or Radio Shack). Check blood pressure and pulse daily, preferably standing and lying flat, and record it. Also check blood pressure when you have symptoms.
2. If possible, eliminate medications that lower blood pressure (usually blood-pressure or heart medications). Check with your doctor first, however, to be sure that this is safe.
3. Take in extra amounts of salt - about 10 gm/day total. Another way to get extra salt is to use salt containing beverages (e.g. "gatorade"). If you start to have trouble breathing or get excessive swelling at the ankles, you may have to use less than 10 gm. Similarly, be careful not to overdo it and end up with hypertension.
4. Wear Jobst stockings or compression stockings custom made leotard like garment -- worn by both men and women). These are often not well tolerated, especially in the summer.
5. Sleep with head of bed elevated about 15-20 degrees (4-6 inches). This maneuver increases blood volume and, after a few days, is helpful. It is also helpful in that it may reduce supine hypertension (sometimes blood pressure is too high lying flat, and too low standing up). Try to be up during the day, not lying in bed. Reconditioning may be helpful for persons who have been on bed rest for long periods of time.
6. Eat frequent small meals (because eating lowers blood pressure). Avoid sudden standing after eating.
7. Avoid straining at stool (because this may lower the blood pressure)
8. Avoid hot showers or excessive heat. Use air conditioners.
9. Get up gradually in the morning. Take 5 minutes to get up and use support. Perform isometric exercises before moving about.
10. Orthostatic training. Under the supervision of a physical therapist, gradually increased upright stance

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DRUG TREATMENT for Orthostatic Hypotension

Certain medications may be helpful, usually as a combination. Most useful drugs are Florinef (fludrocortisone), erythropoetin and Midodrine.

- Two strong cups of coffee in the morning
- Fludrocortisone (Florinef) forces more salt into the bloodstream, 0.1 mg daily starting dose. Blood pressure raises gradually over several days with maximum effect at 1-2 weeks. Alter doses at weekly or biweekly intervals. Hypokalemia (low potassium) occurs in 50%, and hypomagnesemia in 5%. These may need to be corrected with supplements. Florinef should not be used in persons with CHF (congestive heart failure). Florinef does not work in the orthostatic intolerance syndrome of chronic fatigue syndrome (Rowe et al, 2001). Headache is a common side effect.
- Effexor (an antidepressant which raises blood pressure as a side effect).
- Inderal and other beta-blockers (small doses are used for positional-orthostatic-tachycardia syndrome (POTS), start inderal at 10 mg/d, increase to 30-60 mg/d over 2-3 weeks. Other useful agents are Nadolol (10 mg qd), Pindolol (2.5-5 mg 2-3 times/day) and atenolol (25). Several controlled trials did not show these agents to be effective in preventing syncope (Kapoor, 2003)
- Motrin or Indocin (blocks blood-pressure lowering effects of prostaglandins).
- Midodrine. An alpha-1 adrenergic agonist. Causes increased blood pressure, vasoconstriction, pupil dilation, and "hair standing on end". Other common side effects are paresthesia of the scalp or itching. Usual doses are 2.5 mg at breakfast and lunch or three times daily. Doses are increased quickly until a response occurs or a dose of 30 mg/day is attained (Wright et al, 1998). Midodrine levels peak at about 1-2 hours after administration, and have a half-life of about 3-4 hours. Midodrine does not cross the blood-brain barrier and it is thus not associated with CNS effects. In theory, Midodrine might work for the orthostatic hypotension of MSA (or Shy-Drager), but not that of Parkinsonism. Most patients on Midodrine also take Florinef (see above). Midodrine has been shown to be helpful in controlled trials (Kapoor, 2003).
- Erythropoietin. This agent is used if there is also anemia and other measures have failed. Doses of 25 to 75 U/kg TIW are used, by injection.
- Methylphenidate 5-10 mg orally 3 times/day given with meals. An amphetamine -- side effects may include agitation, tremor, insomnia, supine hypertension.
- Ephedrine 12.5-25 mg orally three times/day. Side effects may include tachycardia, tremor and supine hypertension.
- Fluoxetine 10-20 mg daily. Side effects may include nausea and anorexia. Paroxetine (Paxil) has also been shown to reduce syncope at 2 years.
- Phenobarbital may improve POTS.

- Desmopressin. This analog of vasopressin is used as a nasal spray. Low blood sodium is a possible side effect.

Neurogenic orthostatic hypotension is an incapacitating symptom of central and peripheral autonomic nervous system degeneration. It occurs in such clinical conditions as multiple system atrophy, pure autonomic failure, and small-fiber peripheral neuropathies. Although many treatments are available, their effects are inconsistent, unsustained, and complicated by side effects. ***3,4-Dihydroxyphenylserine*** *is a synthetic, unnatural amino acid that is an immediate norepinephrine precursor. There is theoretical and clinical evidence supporting the use of this agent in the treatment of neurogenic orthostatic hypotension in patients with peripheral and central autonomic nervous system dysfunction. We review the biochemistry, pharmacokinetics, and possible mechanisms of action and clinical utility of this agent in the treatment of neurogenic orthostatic hypotension.*

CONCLUSION: DL-DOPS improved features of neurogenic orthostatic hypotension in patients with central and peripheral autonomic nervous system disease. There was an increase in plasma norepinephrine. No major side effects occurred.

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Amino acid precursors to catecholamine (norepinephrine and epinephrine) synthesis: L-phenylalanine and L-tyrosine are building blocks for the catecholamines. Vitamin B6 (P5P form) is a cofactor for the conversion of L-dopa to dopamine.

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Abstract Neurogenic orthostatic hypotension is a cardinal feature of generalised autonomic failure and commonly is the presenting sign in patients with primary autonomic failure. Orthostatic hypotension can result in considerable morbidity and even mortality and is a major management problem in disorders such as pure autonomic failure, multiple system atrophy and also in Parkinson's disease. Treatment is ideally two pronged, using non-pharmacological and pharmacological measures.
Drug treatment ideally is aimed at restoring adequate amounts of the neurotransmitter noradrenaline. This often is not achievable because of damage to sympathetic nerve terminals, to autonomic ganglia or to central autonomic networks. An alternative is the use of sympathomimetics (that mimic the effects of noradrenaline, but are not identical to noradrenaline), in addition to other agents that target physiological mechanisms that contribute to blood pressure control. L-threo-dihydroxyphenyslerine (Droxidopa) is a pro-drug which has a structure similar to noradrenaline, but with a carboxyl group. It has no pressor effects in this form. It can be administered orally, unlike noradrenaline, and after absorption is

converted by the enzyme dopa decarboxylase into noradrenaline thus increasing levels of the neurotransmitter which is identical to endogenous noradrenaline. Experience in Caucasians and in Europe is limited mainly to patients with dopamine beta hydroxylase deficiency. This review focuses on two studies performed in Europe, and provides information on its efficacy, tolerability and safety in patients with pure autonomic failure, multiple system atrophy and Parkinson's disease. It also addresses the issue of whether addition of dopa decarboxylase inhibitors, when combined with l-dopa in the treatment of the motor deficit in Parkinson's disease, impairs the pressor efficacy of Droxidopa.

Key words l-dihydroxyphenylserine - orthostatic hypotension - autonomic failure - noradrenaline - multiple system atrophy - Parkinson's disease

http://en.wikipedia.org/wiki/Droxidopa

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Ruscus aculeatus (Butcher's Broom) as a Potential Treatment for Orthostatic Hypotension, with a Case Report

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Context: Chronic orthostatic hypotension (OH) is frequently a severely debilitating disease that affects large groups of the population with autonomic insufficiency—the elderly; patients with diabetes, Parkinson's disease, and chronic fatigue syndrome; and anyone on drugs that affect the autonomic nervous system. Unfortunately, even though more than 60 medications are currently being used to treat OH, none of them is particularly or consistently effective. *Ruscus* aculeatus, a phytotherapeutic agent that is well known in Europe, may, however, change this. Its vasoconstrictive and venotonic properties make it ideally suited to treat the pooling of blood in the limbs, lack of venous tone, and lack of neurally mediated vasoconstriction that frequently characterize OH. Although it has never been suggested as a treatment for OH, it already has a long, proven record of use in Europe for treating a variety of circulatory disorders.

Objective: To provide evidence for what appears to be an effective, safe, inexpensive botanical therapy for OH and encourage further studies on the efficacy of *Ruscus* for OH patients.

Design: Review of OH and therapies currently available for OH and evaluation of the properties of *Ruscus aculeatus*, its mechanism of action, and its suitability as a therapeutic agent for treatment of OH.

Results: A review of the many pharmacologic and nonpharmacologic agents for treating OH reveals that all of the drug therapies are disappointing and marginally useful. Although nonpharmacologic management is preferred, in the many cases in which OH becomes debilitating, pharmacologic intervention becomes a last resort. But drug therapy may not always

be necessary, because *Ruscus aculeatus*, a phytotherapeutic agent containing ruscogenins and flavonoids, may prove useful for the treatment of OH if denervation is not so advanced that it has compromised receptor activity at the venous wall. *Ruscus aculeatus* is an *α*-adrenergic agonist that causes venous constriction by directly activating postjunctional α_1- and α_2-receptors, in turn stimulating the release of noradrenaline at the level of the vascular wall. It also possesses venotonic properties: it reduces venous capacity and pooling of blood in the legs and exerts protective effects on capillaries, the vascular endothelium, and smooth muscle. Its flavonoid content strengthens blood vessels, reduces capillary fragility, and helps maintain healthy circulation. Unlike most of the drug therapies used to treat OH, *Ruscus aculeatus* does not cause supine hypertension. It also appears to do something no other therapy can offer—alleviate the worsening effects of OH in environmentally hot conditions. Finally, it is an extremely safe, inexpensive, over-the-counter botanical medicine.

Conclusion: With proven phlebotherapeutic properties, including vasoconstrictive action and venotonic properties, *Ruscus aculeatus* shows great promise for ameliorating the symptoms of OH and improving the quality of life for large groups in the population. It clearly deserves to be the object of wider research and study as a treatment for OH.

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ABSTRACT

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