Normalization of Blood Pressure in a Patient With Severe Orthostatic Hypotension and Supine Hypertension Using Clonidine

To the Editor:

A 78-year-old woman presented to us with a 4-year history of recurrent dizzy spells, which had increased in frequency over past 12 months. Past medical history included hypertension and glaucoma. Current medications were oral perindopril (an ACE inhibitor), aspirin, and 3 eye drops—brimonidine (a $\alpha_2$-adrenergic agonist), betaxolol (a topical $\beta_1$-adrenergic blocking agent), and latanoprost (a selective prostanooid $\mathrm{FP}_1$-receptor agonist)—for glaucoma.

Cardiovascular examination revealed an aortic ejection systolic murmur; supine blood pressure was 180/100 mm Hg. There was no clinical evidence of autonomic dysfunction, parkinsonian features, or gross neurological abnormalities.

She had 4 presyncopal episodes over 5 days, with no arrhythmia on telemetry. She had mild aortic stenosis (peak and mean gradients of 19 and 11 mm Hg, respectively) and normal left ventricular function by echocardiography. Exercise stress test was negative. Tilt table test and routine blood pressure observations revealed significant postural hypotension (180/100 mm Hg supine to 120/90 mm Hg erect with no significant change in her heart rate).

Treatment with oral perindopril was stopped after 4 days because of worsening of postural drop and continuing symptoms. Brimonidine tartrate is a $\alpha_2$-adrenergic agonist that is 1000 times more selective for $\alpha_2$-adrenoceptors than the $\alpha_1$-adrenergic receptor. Topical administration of brimonidine tartrate decreases intraocular pressure with minimal effects on cardiovascular parameters, although bradycardia and hypotension are known to occur in neonates. Caution is advised with concomitant use of sympathomimetic agents or agonists or antagonists of adrenergic receptor because brimonidine eye drops may reduce blood pressure.1 Betaxolol hydrochloride is a topical $\beta_1$-adrenergic blocking agent that has been shown to have a minor effect on heart rate and blood pressure in clinical studies; caution is advised in treating patients with a history of cardiac failure or heart block.1 Latanoprost is a selective prostanooid $\mathrm{FP}_1$-receptor agonist that reduces intraocular pressure with no adverse effects on heart rate or blood pressure.1 The combination of brimonidine and betaxolol eye drops could have contributed to her symptoms. Betaxolol eye drops were stopped with little effect on her blood pressure. We could not stop both her eye drops because of the fear of making her glaucoma worse. Thus, she presented with a not uncommon but vexing problem of severe supine hypertension with symptomatic postural hypotension. The use of standard agents (eg, fludrocortisone or midodrine2–4 for postural hypotension may have resulted in worsening of her hypertension.

She was started on low-dose clonidine (50 $\mu$g/m/d), with almost immediate and marked improvement in both her supine hypertension and postural hypotension and with cessation of presyncopal episodes within 24 hours. By 48 hours, there was virtually no postural drop in blood pressure with good control of hypertension (136/70 mm Hg), and she was symptom free. She was discharged home on clonidine therapy (50 $\mu$g/m/d) and has remained well since.

Clonidine has a predominant central action on $\alpha_2$-adrenoceptors. This results in the inhibition of bulbar sympathetically cardio-accelerator and sympathetic vasoconstrictor centers and, thereby, a decrease in heart rate. There is also an increase in baroreceptor activity that leads to reduction in blood pressure. Additionally, it acts on peripheral postsynaptic $\alpha_2$-adrenoceptors and also stimulates peripheral $\alpha_1$-adrenergic receptors, leading to vasoconstriction, increased venous return, and increased blood pressure.

There are limited previous reports on its use in the treatment of orthostatic hypotension.5,6 Robertson et al5 tried higher doses (400 to 800 $\mu$g/m) in 4 patients with severe idiopathic orthostatic hypotension with good results. They postulated that the predominance of the pressor response over the depressor effect may have been due to a reduction in sympathetic outflow in elderly patients, and low circulating catecholamine levels were documented. A combination of these 2 opposing effects may have led to the normalization of blood pressure in our patient.

We suggest that clonidine should be considered as a possible agent in the treatment of symptomatic idiopathic orthostatic hypotension concomitant with supine hypertension.

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