Orthostatic Hypotension and Supine Hypertension in Primary Autonomic Failure
To the Editor:

We read with interest the article of Shibao et al dealing with the treatment options when neurogenic orthostatic hypotension is complicated by supine hypertension.1

When orthostatic hypotension is caused by central and peripheral nervous system disorders such as primary autonomic failure, the patients report several syncope episodes, and treatment of hypertension is a “dilemma.” In the “management of supine hypertension” section, the authors propose a stepwise approach to treat hypertension, including the use of antihypertensive agents in patients with pure autonomic failure (PAF) and multiple system atrophy.

Because it is more important to avoid daytime hypotension than hypertension, we suggest caution in the use of antihypertensive agents. The physician in charge should remember that the decision of starting antihypertensive drugs should not be based on the blood pressure values measured while the patient is lying in bed in the hospital. In case of supine hypertension, laboratory investigation, resting electrocardiography, echocardiography, and ultrasound carotid examination should be performed according to recent guidelines for the management of arterial hypertension.2 Moreover, a 24-hour noninvasive ambulatory blood pressure measurement (ABPM) should be included in the clinical assessment because it correlates strictly with target organ damage,3,3 and it can show the real blood pressure pattern during everyday life.

The documentation of hypertensive target organ damage suggests that one should undergo antihypertensive drug treatment. In patients with PAF, whose life expectancy is only a little reduced,4 prevention of cardiovascular events with antihypertensive agents is reasonable, whereas in patients with multiple system atrophy, whose survival is considerably poorer than in PAF,4 antihypertensive therapy is questionable and may be deferred.

In our series, 3 patients with neurogenic orthostatic hypotension caused by PAF had supine hypertension, also in the absence of pharmacological therapy.5 All the patients presented hypertensive target organ damage, and short-acting dihydropyridine–calcium antagonists were given at night. In 1 patient, salt-retaining steroid fludrocortisone worsened supine and nocturnal hypertension, as shown by blood pressure values measured at ABPM (Figure), and a transient ischemic attack occurred. When fludrocortisone was downtitrated and transdermal nitroglycerin associated to short-acting antihypertensive calcium antagonist, the patient did not further report symptoms.

In conclusion, antihypertensive agents should not be used in all patients with supine hypertension and PAF but limited to those patients with hypertensive target organ disease or with sustained nocturnal hypertension.

Michelangelo Sartori
Achille C. Pessina
Andrea Semplinici

Department of Clinical and Experimental Medicine
University of Padua
Padua, Italy


Response:

We are grateful for the interest Dr Sartori and colleagues expressed in our article and welcome the opportunity to clarify some of the concepts included in it. We concur with most, but not all, of the comments made by Sartori et al. We agree about the importance of management guidelines for essential hypertension, but we believe they cannot be applied blindly to patients with autonomic failure. Although tempting, fixed recommendations are difficult to make in this patient population, and treatment should be individualized. The difficulties in the management of this problem can be summarized in three questions: (1) Why should these patients be treated? (2) Who should be treated? and (3) How should they be treated?

Why?

We argue that supine hypertension may actually worsen orthostatic hypotension by inducing pressure diuresis and volume depletion, as documented several years ago.12 This is the basis for recommending patients to avoid the supine position during the day. This phenomenon itself would be reason enough to treat supine hypertension during the night if we could find an antihypertensive that reduces nighttime diuresis. So far, we have not been successful, but potentially useful drugs are under investigation.
Who?

A second reason to treat these patients is to avoid end-organ damage and the long-term consequences of hypertension. As suggested by Sartori, supine hypertension can be treated less aggressively in patients with multiple system atrophy, considering their reduced life expectancy. However, this should not be taken as an absolute rule, and the severity of hypertension and other clinical characteristics should be considered. Certainly, these patients can be treated with the nonpharmacological measures outlined in our review. It is true that there is no experimental proof that antihypertensive medications will improve survival in autonomic failure patients, and given the rarity of this condition, we do not foresee that evidence-based medical decisions will be forthcoming. On the other hand, we believe that supine hypertension can be treated without worsening orthostatic hypotension.

How?

Sartori et al are justifiably concerned that using antihypertensives will worsen daytime orthostatic hypotension in patients with autonomic failure. We do agree with them that improving quality of life should be paramount in management decisions. It is precisely for this reason that we recommend using a stepwise approach to their treatment, with antihypertensives used as the last resource. Even then, they should be taken only at night, using short-acting antihypertensives to minimize a carryover hypotensive effect to the daytime. Initial management should include eliminating drugs that may worsen supine hypertension. As mentioned in our review, this includes avoiding pressor agents late in the day, and fludrocortisone, as illustrated in the example presented by Sartori et al.

We agree that 24-hour blood pressure monitoring can be very helpful in these patients, but data need to be interpreted carefully. This technique is particularly useful in determining the severity of nighttime hypertension and whether it is sustained throughout the night; some patients may start with severe hypertension at bedtime but may “dip” during the night to normotensive levels. These patients may not require treatment. Ambulatory blood pressure monitoring is also useful in determining the effectiveness of antihypertensive treatment and in dose titration. Blood pressure monitoring is less useful during the daytime because blood pressure will fluctuate considerably with posture, increasing to hypertensive levels if patients lie down and decreasing considerably if they stand up, and with seemingly trivial interventions such as meals or water drinking. The average 24-hour blood pressure is arguably the best predictor of end-organ damage in patients with essential hypertension, but its predictive value may be lost in patients with autonomic failure because of this variability. For instance, in the Hypertension and Ambulatory Recording Venetia Study (HARVEST), ambulatory blood pressure was a better predictor of end-organ damage than office blood pressure only in subjects with a reproducibility between monitoring days of <4 mm Hg.

Cyndya Shibao
Alfredo Gamboa
André Diedrich
Italo Biaggioni

Division of Clinical Pharmacology
Department of Medicine and Pharmacology
and the Autonomic Dysfunction Center
Vanderbilt University School of Medicine
Nashville, Tennessee
