Pressor Effects of $\beta$-Blockers on Standing Blood Pressure May Be Harmful for Older Patients With Orthostatic Hypertension

To the Editor:

Cleophas et al. reported an interesting pressor effect of $\beta$-blockers in elderly patients with mild hypertension on standing such that pulse pressure, which decreased on standing when treated, showed an increase after $\beta$-blockade. Although they considered this pressor effect to be beneficial, we think that this is not always the case.

The orthostatic blood pressure (BP) reaction varies greatly among older individuals. In addition to orthostatic hypotension, which is a well-known risk factor for falls, syncope, and cardiovascular events in the elderly, in a recent study, we found orthostatic hypotension to be a new risk factor for stroke in elderly hypertensive patients. We performed a head-up tilt test and brain MRI in 241 elderly subjects with sustained hypertension confirmed by ambulatory BP monitoring. We classified the patients into an orthostatic hypertension group with an orthostatic increase of systolic BP (SBP) of ≥20 mm Hg (n=26), an orthostatic hypotension group with an orthostatic SBP decrease of ≥20 mm Hg (n=23), and a normal group with neither of these 2 patterns (n=192). Silent cerebral infarcts detected by brain MRI were more common in the orthostatic hypertension (3.4 per person, P<0.0001) and orthostatic hypotension groups (2.7 per person, P=0.04) than in the normal group (1.4 per person). Thus, we think that the pressor effect of $\beta$-blocker could be potentially harmful for the elderly hypertensive patients with orthostatic hypotension.

In our study, the orthostatic BP increase found in the elderly hypertensive patients with orthostatic hypertension was selectively abolished by $\alpha$-adrenergic blockade. This result indicates that $\alpha$-adrenergic activity is the predominant pathophysiological mechanism of orthostatic hypotension. As mentioned by Cleophas et al., this pressor effect of $\beta$-blockers might be because of the imbalance between $\alpha$-adrenergic vasoconstrictor activity and $\alpha$-adrenergic vasodilator activity. In our study, morning SBP, which is predominantly determined by $\alpha$-adrenergic activity, was higher in the orthostatic hypertension group than in the normal group (159 versus 149 mm Hg, P=0.007), whereas there were no significant differences in ambulatory BP between the 2 groups during other periods. Thus, $\beta$-blockers might further enhance the increased orthostatic BP response in elderly hypertensive patients with orthostatic hypertension and $\alpha$-adrenergic hyperactivity, particularly in the morning. The morning surge of BP coincides with the time of greatest susceptibility to stroke and other cardiovascular events.

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Response

The letter to the editor by Kario et al on the pressor effects of tilting on elderly patients is interesting and relevant to the subject of our recently published paper. Contrary to what Kario et al said, however, we did mention the theoretical disadvantage of the pressor effect of $\beta$-blockers in elderly subjects without orthostatic hypotension. In our study, however, this category must have been very small, considering the homogeneous effects and small confidence intervals in our data. Baroreflex sensitivity declined with age, reversing a pressor effect on systolic blood pressure and pulse pressure while standing into a depressor effect. In patients aged between 50 and 60 years, systolic blood pressures did not rise on standing, and even started to fall, whereas diastolic pressures remained largely unchanged. This effect was greater in older age groups, and was accompanied by a decrease in pulse pressures. Increased rigidity of the arterial wall was probably involved. Thus, we presume that Kario et al are talking about a rare category of patients that may not be so relevant for the entire population of elderly patients with hypertension.

The authors observed elderly patients with pressor or with depressor effects on tilting, and suggest that the former category may be at risk of severe pressor effects on $\beta$-blockers. This is not necessarily the case, however, and largely depends on whether they have increased sympathetic activity. So far, the pressor effect of $\beta$-blockers has exclusively been observed in situations of increased sympathetic activity. Examples include hypoglycemia, pheochromocytoma, cocaine abuse, various stress tests, epinephrine infusions, and hyperadrenergic orthostatic hypotension. It is true that large samples of the elderly have, generally, a slightly increased sympathetic activity. However, if sympathetic efferents are intact, elderly patients with orthostatic hypotension will be more at risk of pressor effects from $\beta$-blockers than will those with orthostatic hypertension. The authors found a slightly increased incidence of silent cerebral infarction in the group with orthostatic hypertension and suggest that the pressor effect may be responsible. However, the slightly increased incidence might be because of chance or because of a variety of uncontrolled risk factors.

We believe, therefore, in the beneficial effect of the pressor effect. In our hands, long-term $\beta$-blockade effectively reduced blood pressure by 24/14 and 14/8 mm Hg in patients aged >60 years who were previously untreated and treated, respectively. Nonetheless, although the antihypertensive potential was maintained, a depressor effect was offset and turned into a mild pressor effect by long-term $\beta$-blockade. This effect was not observed with other classes of drugs, including renin angiotensin inhibitors, calcium channel blockers, and diuretics. Our data could, therefore, have practical implications for future hypertension research, and for the pharmacological treatment of hypertension in the elderly.

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