Amlodipine and Stroke Prevention

To the Editor:

We enjoyed the article by Wang et al1 dealing with prevention of stroke and myocardial infarction by amlodipine and angiotensin receptor blockers. Wang et al1 have confirmed previous meta-analyses showing that calcium channel blockers (CCBs) provide the highest protection against stroke and myocardial infarction when compared with other antihypertensive agents. The authors concluded that blood pressure control seems to be the main therapeutic mechanism but did not reject the possibility that blood pressure-independent influence could account for differences between drugs. They suggested that further evaluation of angiotensin receptor blockers should be designed in view of previous reports suggesting that amlodipine benefit over other antihypertensive agents could result from a better control of central aortic pressure.

Hemodynamic properties of CCBs are classically attributed to arteriolar vasodilation.2 Variations in regional sensitivity to vasodilatatory effects of CCBs are well documented and may be related to their tissue selectivity.2 It is worth mentioning that therapeutic regimens of CCBs evoke a reduction of blood pressure more pronounced in hypertensive than in normotensive subjects. Consistently, spontaneous hypertensive rat vessels, which have an exquisite Ca-dependent tone, exhibit increased responsiveness to vasoconstrictors, as well as to the tissue-selective vasorelaxant action of CCBs.2 We hypothesize that tissue selectivity of CCBs, a factor regulating differently the arterial perfusion in the various vascular beds, might account for the difference in brachial and central aortic pressures.

Blood pressure–independent effects of CCBs are believed to be involved in the protection of stroke-prone spontaneous hypertensive rats exposed to salt load. They are composed of the prevention of overproduction of endothelin-1 in vessel walls, inhibition of endothelin-1 vasoconstriction in small arteries, remodeling of cerebral vessels, antioxidant effects, and interaction with the L-arginine-NO pathway.3 Indeed, amlodipine directly promotes endothelial NO synthase activation by vasodilator agonists by decreasing its interaction with inhibitory caveolin-1.4 Potentiation of vascular endothelial NO synthase activity decreases systolic blood pressure variability,4 a parameter closely related to target organ damage that could also explain the differential effect of antihypertensive drugs, at least in animals.3 Evaluation of the contribution of such pharmacological properties to the prevention of stroke in patients deserves further investigation.

Disclosures

None.

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