Aldosterone and Large Artery Vessels

To the Editor:

We congratulate Dr Schiffrin for his excellent review on the effects of aldosterone on the vasculature.1 Recent reports have clearly demonstrated the endocrine properties of aldosterone have assumed a broader perspective, with nonclassic actions acting on nonepithelial cells and in nonrenal target tissues including the heart and the kidney. Dr Schiffrin extends this formulation to the aldosterone effects on the vasculature. These effects, however, modulate large-artery elasticity with consequent clinical implications, which were not discussed in the review.

The effects of aldosterone and the selective aldosterone antagonist eplerenone on the mechanical properties of the carotid artery have been investigated in vivo.2 By comparison with controls, aldosterone was administered in uninephrectomized Sprague-Dawley rats fed a high-salt diet. Aldosterone induced higher systolic and pulse pressures, with minor changes of diastolic blood pressure, and enhanced carotid elastic modulus (Einc), medial cross-sectional area (MCSA), and aortic fibronectin. No change of wall stress or elastin and collagen densities occurred. No differences in collagen mRNA levels were detected between groups. Treatment with eplerenone blunted the pulse pressure increase in aldosterone-treated rats and normalized the Einc-wall stress curves, MCSA, and fibronectin. The effects were dose-dependent and not accompanied by a reduction of wall stress. Thus, under high-sodium diet, aldosterone increased carotid arterial stiffness in association with accumulation of aortic fibronectin, but independently of wall stress. Eplerenone completely reversed the arterial stiffness changes.

Aortic fibronectin isoform protein, which is specifically produced within the vascular wall, was increased in aldosterone-salt animals compared with controls.2 This increase was specific, because it was not associated with a concomitant increase in collagen expression, which was already present in the myocardium at the same period.2 Endothelin, which is stimulated by aldosterone, is also able to induce vascular fibronectin and could play a role in the pathogenesis of increased stiffness.1 On the other hand, aortic fibrosis in normotensive and hypertensive rats was shown to be prevented by spironolactone alone, independent of age.3

The aldosterone-induced changes in arterial stiffness have important clinical implications. In patients with hypertension, increased plasma aldosterone levels are negatively associated with reduced large vessel compliance, independently of age or blood pressure.4 The aldosterone-induced target organ damage may be enhanced in the presence of gene polymorphisms related to aldosterone.5 In hypertensive subjects, the TC and CC genotypes of the CYP11B2 gene polymorphism involve, by comparison with the TT genotype, significantly higher values of plasma aldosterone and aortic stiffness. Whether this polymorphism participates in mediating systolic hypertension in the elderly remains to be established. Because the same genotype is associated with a reduction of stroke volume, which favors a decrease in systolic blood pressure, and because increased arterial stiffness has an opposite effect on systolic blood pressure, no increased incidence of systolic hypertension would be anticipated.5

We propose that consideration of the actions of aldosterone to modulate large artery elasticity and its consequent clinical implications would enhance our understanding of the widespread effects of aldosterone throughout the vasculature.

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