Letter by Campbell Regarding Article, “Statin Use and Adrenal Aldosterone Production in Hypertensive and Diabetic Subjects”

To the Editor:

Baudrand et al reported that statin use was associated with lower plasma aldosterone levels and urinary aldosterone excretion in non-randomized studies of hypertensive and diabetic subjects, both in the basal state and during stimulation by angiotensin II infusion or by a low sodium diet. They also reported that 10 μmol/L statins, a concentration that far exceeds peak plasma statin concentrations in patients, reduced the aldosterone secretory response of rat zona glomerulosa cells to angiotensin II and to potassium stimulation in vitro, and proposed that statins might reduce plasma aldosterone levels and urinary aldosterone excretion by inhibiting aldosterone steroidogenesis. However, mechanisms other than a direct effect of statins on aldosterone steroidogenesis should be considered.

Baudrand et al reported no effect of statins on plasma cortisol levels or urinary cortisol excretion, but they did not measure plasma adrenocorticotropic hormone (ACTH) levels or examine the effects of statin therapy on ACTH-stimulated cortisol secretion. In a within-patient, placebo-controlled study, Mol et al found that simvastatin reduced basal plasma cortisol levels and increased basal plasma ACTH levels, thereby demonstrating that the effect of statin therapy on plasma cortisol levels needs to be examined in relation to factors that regulate cortisol secretion, such as ACTH. The effect of statins on aldosterone secretion should be similarly examined in relation to known regulators of aldosterone secretion, such as the renin angiotensin system and potassium. Baudrand et al state that “the aldosterone-to-renin ratio was not different when analyzed by statin use on both high and low salt diet,” which suggests that the effect of statins on basal aldosterone levels was explained, at least in part, by lower plasma renin activity in statin users not receiving antihypertensive therapy. It would be of interest to know whether plasma potassium concentrations were different between statin users and nonusers in their study of hypertensive subjects not receiving antihypertensive therapy.

An additional mechanism by which statins may reduce aldosterone synthesis is the reduction in plasma low-density lipoprotein concentrations by statin therapy. Kovanen et al showed that adrenocortical cells obtain cholesterol for steroid synthesis from receptor-mediated uptake of plasma low-density lipoproteins. Moreover, rat zona glomerulosa cells show depletion in cholesterol ester content when stimulated by potassium, and potassium-stimulated aldosterone production by rat zona glomerulosa cells is enhanced when they are incubated in the presence of low-density lipoproteins, indicating that cholesterol supply for steroidogenesis is rate limiting when aldosterone secretion is stimulated. Thus, statins may lower aldosterone secretion by reducing plasma low-density lipoprotein concentrations and reducing cholesterol supply for steroidogenesis. There are, therefore, several mechanisms by which statins could reduce aldosterone secretion other than by a direct effect on aldosterone steroidogenesis.

Disclosures

None.

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References


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