Captopril Test Can Give Misleading Results in Patients With Suspect Primary Aldosteronism

To the Editor:

Primary aldosteronism (PA) has emerged as the most common form of secondary hypertension.1 The widespread use of the plasma aldosterone/plasma renin activity ratio as a screening test for both hypokalemic and normokalemic hypertensive subjects has allowed the demonstration of a high prevalence of this disease, with PA accounting for up to 5% to 10% of all hypertensive patients.1,2 The diagnosis of PA is of particular importance for the clinician, because it has been demonstrated recently that patients with PA are more prone to cardiovascular and cerebrovascular complications, and to target organ damage compared with essential hypertensive subjects with similar risk profiles.3

A positive plasma aldosterone concentration/plasma renin activity ratio should always be followed by a suppression test to definitively confirm the diagnosis. The confirmatory diagnosis is usually made with a saline load test (SLT; oral or intravenous) or with the fludrocortisone suppression test (FST).1 Confirmation of the diagnosis of PA should subsequently undergo a computed tomography scan and adrenal venous sampling to distinguish the subtype of PA.1 A captopril test has also been used both as a screening test and, in some circumstances, as a confirmatory test.

We recently performed a study comparing the SLT with the FST in 100 patients with a positive screening test.4 We report here the results of the captopril test as a confirmatory test in 11 patients in whom SLT and FST displayed concordant results. The captopril test was performed ≥3 weeks after the previous tests, between 8 AM and 10 AM, with the subject in the sitting position in a quiet room. Plasma aldosterone concentration and plasma renin activity were measured before and 2 hours after administration of captopril (50 mg). Selection of the patients, diet, therapy, and hormone measurements is described in detail elsewhere.4 Patients were advised to maintain a diet with normal and constant sodium intake (120 mmol of sodium and 60 mmol of potassium per day). All antihypertensive drugs were stopped ≥3 weeks before the screening test, ≥6 weeks for diuretics and ≥8 weeks for spironolactone). In patients for whom treatment could not be withdrawn for ethical reasons, an α-blocker (doxazosin) and/or a calcium channel blocker (verapamil) were used for blood pressure control, and the same therapy was maintained throughout the tests.

Six patients who had confirmed PA with both FST and SLT underwent a computed tomography scan and adrenal venous sampling. Three patients had bilateral adrenal hyperplasia, and another 3 patients had an aldosterone-producing adenoma. Five patients with both a negative SLT and FST were considered to be essential hypertensive subjects. Five of 6 patients with PA displayed an plasma aldosterone/plasma renin activity ratio postcaptopril >30 ng dL⁻¹/ng mL⁻¹ h⁻¹, but 1 patient with aldosterone-producing adenoma displayed an plasma aldosterone/plasma renin activity ratio postcaptopril <30 and an aldosterone <8.5 ng/dL and, therefore, would have been missed relying only on the captopril test.5 This patient displayed an increase of aldosterone levels >50% of the basal level during the posture test, indicating an angiotensin II–responsive adenoma. By contrast, 3 of 5 patients who displayed a normal suppression of aldosterone after SLT and FST and, therefore, were classified as being affected by essential hypertensives, displayed a plasma aldosterone/plasma renin activity ratio postcaptopril of >30. These patients would have unnecessarily undergone computed tomography scan and adrenal venous sampling relying only on the captopril test, thereby resulting in increased costs and discomfort for the patients.

The captopril test has been compared previously with the oral saline load in a group of hypertensive patients with spontaneous hypokalemia and, therefore, at very high risk of PA.5 In fact, 44 of 49 were found to be affected by PA, and for this reason, the authors only discussed the sensitivity and not the specificity of the captopril test. Two aspects should be considered to explain the different findings between our study and the study of Agharazi et al:4 first, in our study, only 2 patients (1 aldosterone-producing adenoma and 1 bilateral adrenal hyperplasia) were hypokalemic, whereas Agharazi et al studied only hypokalemic patients and, therefore, could have underestimated the possibility of false-negative results in patients with a mild form of PA; second, a proportion of false-positive patients could have been found by Agharazi et al if they had studied a larger population of essential hypertensive subjects.

The present data need to be confirmed prospectively in a larger population. However, our findings indicate that, at least in some cases (4 of 11 [36%] in our study), the captopril test was misleading if used as a confirmatory test for the diagnosis of PA. Therefore, in the absence of contraindications such as reduced cardiac or renal function, saline load or FST should be preferred to the captopril test for the confirmatory diagnosis of PA.

Disclosures

None.

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