

Renin-Aldosterone Studies

A. Renin-Angiotensin-Aldosterone System:

1. Renin is secreted by the juxtaglomerular cells of the kidneys in response to changes in plasma volume. An increase in renin normally produces an increase in aldosterone through angiotensin intermediates. Renin's physiological effects are manifested mainly through its changes on aldosterone production. Aldosterone is produced by the adrenal glands and fluctuates normally with changes in renin levels. With aldosterone-producing tumors, the serum aldosterone level is elevated even though renin is suppressed. Aldosterone production results in retention of sodium and excretion of potassium.

B. Usual Laboratory Test Findings in Renin-Aldosterone Disorders:

1. Renal disease, such as unilateral renal artery stenosis, results in elevated renin and aldosterone levels. Renal venous catheterization may be helpful. A positive test is a renal venous renin ratio (affected/normal) >1.5.
2. Primary aldosteronism is manifested by low renin and elevated aldosterone levels. The aldosterone level will not be suppressed by a high salt intake, whereas in normals it will. An elevated urinary aldosterone excretion rate and increased levels of serum aldosterone associated with low plasma renin activity is presumptive evidence for primary aldosteronism.

C. Preparation of Patient for Plasma Renin Activity Determination:

1. When screening for primary aldosteronism, no preparation is required. The plasma renin activity cannot be interpreted if the patient is being treated with spironolactone (Aldactone®). Spironolactone should be discontinued for 4 to 6 weeks before testing.
2. When performing renal vein renins to investigate renovascular hypertension, the angiotensin converting enzyme (ACE) inhibition protocol may be used.

It has been shown that acute administration of drugs which block the action of ACE will enhance renin lateralization. Surprisingly, the effect is not seen if 3 drugs are given chronically. An advantage of this protocol is that the inhibiting effects of other drugs can be eliminated, and it is unnecessary to allow a washout period to pass. Captopril (Capoten®—Squibb) is available as a converting enzyme inhibitor. Reports of renal toxicity by a variety of mechanisms are known. It would appear, however, that a single dose for testing purposes is relatively innocuous.

Administer captopril 25 mg by mouth 30 minutes prior to the procedure. Caution should be taken to guard against orthostatic hypotension.

D. Preparation of Patient and Specimens for Primary Aldosteronism Study:

1. Screening testing—the serum aldosterone to plasma renin activity (SA/PRA) ratio
 - a. No salt depletion is necessary.
 - b. Collect a simultaneous blood specimen for serum aldosterone and plasma renin activity before 10 a.m. No special posture instructions are needed. Blood should be drawn in the seated position. The SA/PRA ratio may be performed while the patient is on antihypertensive medications. Spironolactone is the only medication that will absolutely interfere with interpretation of the ratio. ACE inhibitors have the potential to “falsely elevate” PRA. Therefore, in a patient treated with an ACE-inhibitor, the findings of a detectable PRA level or a low SA/PRA ratio do not exclude the diagnosis of primary aldosteronism. In addition, a strong predictor for primary aldosteronism is a PRA level undetectably low in a patient taking an ACE-inhibitor.

A high ratio of SA (in ng/dL) to PRA (in ng/mL/hour) is a positive screening test result, a finding that warrants further testing. An SA/PRA ratio ≥ 20 and SA ≥ 15 ng/dL indicates probable primary aldosteronism.

2. Confirmatory testing—aldosterone suppression testing

An elevated SA/PRA ratio is not diagnostic by itself, and primary aldosteronism must be confirmed by demonstrating inappropriate aldosterone secretion. The list of drugs and hormones capable of affecting the renin-angiotensin-aldosterone axis is extensive. Frequently, in patients with severe hypertension, a “medication-contaminated” evaluation is unavoidable. Calcium channel blockers, α_1 -adrenergic receptor blockers, and β -adrenergic receptor blockers do not affect the diagnostic accuracy in most cases. It is impossible to interpret data obtained from patients receiving treatment with spironolactone. Therefore, spironolactone treatment should not be initiated until the evaluation is completed and the final decisions about treatment are made. If primary aldosteronism is suspected in a patient receiving treatment with spironolactone, the treatment should be discontinued for at least 6 weeks.

Aldosterone suppression testing can be performed with orally administered sodium chloride and measurement of urinary aldosterone or with intravenous sodium chloride loading and measurement of SA. Our practice has been oral salt loading over 3 days. After hypertension and hypokalemia are controlled, patients should receive a high sodium diet (supplemented with sodium chloride tablets if needed) for 3 days. The risk of increasing dietary sodium in patients with severe hypertension must be assessed in each case. Because the high salt diet can increase kaliuresis and hypokalemia, vigorous replacement of potassium chloride should be prescribed. On the third day of the high sodium diet, a 24-hour urine specimen is collected for measurement of aldosterone, sodium, and potassium. The 24-hour urinary sodium excretion should exceed 200 mEq to document adequate sodium repletion. Urinary aldosterone excretion >12 mg/24 hours in this setting is consistent with hyperaldosteronism.