Emerging studies show that beyond a phenotype of overt primary aldosteronism, there exists a prevalent phenotype of renin-independent aldosterone production among patients with low-renin hypertension (LRH). Mineralocorticoid receptor antagonist (MRA) therapy to induce an increase in renin is associated with favorable outcomes in primary aldosteronism. Whether a similar approach is beneficial for all patients with low-renin hypertension is not known. We evaluated whether treatment of patients with LRH with MRAs to increase renin is associated with a decrease in blood pressure and/or proteinuria.

We have conducted a prospective observational cohort study of consecutive patients from the practice of co-author A.T. between 2005 and 2021. Patients were included if they had hypertension with suppressed (< 1.0 ng/ml/h) plasma renin activity (PRA) and detectable aldosterone levels but favored empiric medical therapy over further diagnostic testing. All patients were subsequently treated with an MRA. MRA was started at 25-50 mg daily of spironolactone (women) or eplerenone (men) and the dose was gradually increased in 25-50 mg increments to target a PRA ≥ 1.0 ng/ml/h or the maximal tolerated dose. Blood pressure, albumin-to-creatinine ratio (ACR), and other patient characteristics at baseline vs. after unsuppressed renin was achieved were compared using a paired-samples t-test.

The mean age of 31 study patients who achieved unsuppressed PRA was 67.9 (SD 11.9) and 14 (45.2%) were women. The mean baseline aldosterone was 14.9 ng/dL (SD 9.4); 13 (41.9%) patients had baseline aldosterone < 10.0 ng/dL. Most (21/31; 67.7%) patients had baseline PRA below the assay detection limit. The mean baseline potassium was 4.2 (SD 0.46); one (3.2%) patient had baseline hypokalemia (K < 3.5 mEq/l/dL). The mean final PRA was 4.78 (SD 5.64) ng/ml/h. The median (IQR) MRA dose required to achieve unsuppressed PRA was 75 (50 to 200) mg. The mean systolic and diastolic blood pressure decreased from 144.9 (SD 14.9) and 79.2 mm Hg (SD 15.0) at baseline to 124.7 (SD 11.1) and 71.5 mm Hg (SD 10.8), respectively, after achievement of unsuppressed PRA (P < 0.001 for both). The mean number of anti-hypertensive medications decreased from 3.4 (SD 1.3) at baseline to 2.5 (SD 1.5) after achievement of unsuppressed PRA (P < 0.001). Among the six (19.4%) patients who had proteinuria, the mean ACR decreased from 179.0 (SD 102.1) at baseline to 36.1 (SD 49.2) mg/g after achievement of unsuppressed PRA (P = 0.007). Three (9.7%) and seven (22.6%) patients had to have their MRA dose decreased due to symptomatic hypotension and hyperkalemia, respectively.

These findings suggest that suppressed renin may be sufficient to identify patients who could benefit from MR blockade. Treatment of patients with suppressed renin with sufficient MRA dose to achieve its unsuppression could lower both elevated blood pressure and proteinuria.

Presentation: Sunday, June 12, 2022 12:30 p.m. - 2:30 p.m.