Plasma Aldosterone and Glomerular Filtration in Hypertensive Patients With Preserved Renal Function

Julián Roldán, Pedro Morillas, Jesús Castillo, Helder Andrade, Silvia Guillén, Daniel Núñez, Juan Quiles, and Vicente Bertomeu

Unidad de Hipertensión Arterial, Servicio de Cardiología, Hospital Universitario San Juan, Alicante, Spain

INTRODUCTION

Aldosterone, the main mineralocorticoid synthesized by the adrenal gland, has an essential function in sodium and water homeostasis and urinary excretion of potassium. Nonetheless, it has become evident in recent years that this hormone also has an important pathogenic role in hypertension and vascular remodeling, in left ventricular hypertrophy, and in renal disease, specifically proteinuria and glomerulosclerosis in patients with hypertension. A clear example of this association is primary hyperaldosteronism, a secondary cause of hypertension (HT), in which an increase in plasma aldosterone concentration produces a significant deleterious effect on the heart and vessels and leads to a higher risk of experiencing cardiovascular events.

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decreases, due to activation of the renin-angiotensin-
aldosterone system secondary to the change in
glomerular hemodynamics. This contributes to
greater organ damage, affecting both the kidneys
and heart.1,4 In hypertensive patients with preserved
renal function, however, there are no studies
specifically investigating the association between
aldosterone concentration and renal filtration. The
aim of this study was to analyze the relationship
between plasma aldosterone concentration and the
glomerular filtration rate (GFR) in hypertensive
patients with preserved renal function, after ruling
out hyperaldosteronism.

METHODS

During the period of 2005 to 2008, a prospective
study was conducted in all patients with hypertension
older than 18 years of age referred to the hypertension
unit of our cardiology department. A clinical history
and complete physical examination were performed
in all patients, together with specific laboratory tests
to rule out a secondary cause of hypertension (HT).
Samples for laboratory testing were taken after a 12-
hour fast. The tests included a hemogram and routine
biochemical analyses, thyroid hormones, aldosterone,
the plasma aldosterone-to-plasma renin activity ratio
(ALD/PRA), urinary catecholamines and cortisol,
and microalbuminuria in 24-hour urine. Renal
function was estimated by calculating the GFR with
the Modification of Diet in Renal Disease (MDRD)
formula. Renal dysfunction was established on GFR
values of <60 mL/min. Left ventricular mass was
determined by echocardiography using the Penn
formula.

Patients were excluded if they had a diagnosis of
primary hyperaldosteronism as defined by an
ALD/PRA ratio >30, together with elevated
plasma aldosterone (>20 ng/dL) and a lack of
plasma aldosterone suppression following saline
load during 4 hours. Patients with decreased renal
function (GFR <60 mL/min) were also excluded.
Patients were divided into 2 groups according to the
GFR (60-89 mL/min and >90 mL/min), based on
the chronic renal disease stages established by the
National Kidney Foundation (stages 1 and 2).

Statistical Analysis

Continuous variables are expressed as the mean
(standard deviation), and qualitative variables as
the number and percentage. For the analysis of
correlations between the quantitative variables,
ALD and GFR, the Spearman correlation test was
used, since the variables did not follow a normal
distribution. A multiple linear regression analysis
was then performed, adjusting for age, sex, diabetes
mellitus, smoking habit, dyslipidemia, prior ischemic
heart disease, evolution time of HT, systolic and
diastolic arterial pressure, left ventricular mass
adjusted by body surface area and determined by
echocardiography, and plasma aldosterone
concentrations. Because aldosterone concentrations
did not follow a normal distribution, logarithmic
transformation of this variable was carried out. The
statistical analysis was performed with SPSS, version
13, and differences were considered significant at a P
value of <0.05.

RESULTS

After excluding patients with hyperaldosteronism
and/or GFR <60 mL/min, 186 patients with
hypertension were included (58.1%, men), with
a mean age of 55 (13.4) years. The main clinical
characteristics of the population are presented in
Table.

Of the patients enrolled, 77 had a GFR of >90
mL/min and 109 had a GFR of 60 to 89 mL/
min. Patients with GFR 60 to 89 mL/min showed
significantly higher aldosterone values than the
group with GFR >90 mL/min (20.02 vs 15.3 ng/
dL; P<.05). More patients in the group with lower
GFR had a history of ischemic heart disease, left
ventricular hypertrophy on echocardiographic study,
and elevated plasma N-terminal probrain natriuretic
peptide (NT-proBNP) concentrations (Table). There
were no differences between the 2 groups in the
pharmacological treatment received, except for a
higher use of statins in patients with a GFR of 60
to 90 mL/min that approached significance (32.1%
vs 19.5%; P=.06).

There was a modest negative correlation between
plasma aldosterone concentrations and GFR
(r=−0.196; P<.01), in which higher serum aldosterone
values were associated with lower glomerular
filtration (Figure). After adjusting for several
variables, the multivariate analysis confirmed an
independent association between serum aldosterone
concentrations and the GFR in patients with
hypertension (B=−7.36; P<.001). The other associated
variables included age (B=−0.58; P<.001) and
systolic arterial pressure (B=−0.13; P<.05).

DISCUSSION

The present study yielded an interesting finding
that has not been analyzed in depth previously: an
independent association between plasma aldosterone
concentrations and renal filtration in hypertensive
patients with “normal” renal function, such that the
lower the renal filtration values, the higher the plasma
aldosterone concentration. Although the correlation
was modest, this is the first study describing this
In the last years, considerable attention has been focussed on the contribution of aldosterone to the pathophysiology of HT and cardiovascular disease. Various studies have shown that in comparison to patients with essential HT, patients with primary hyperaldosteronism and elevated aldosterone values have higher rates of albuminuria and worsening renal function\(^5\) as well as a larger number of cardiovascular events and a greater degree of left ventricular hypertrophy and vascular remodeling.\(^6\)

### Table 1. Demographic and Clinical Characteristics of the Population Analyzed

<table>
<thead>
<tr>
<th></th>
<th>Total Population (n=186)</th>
<th>GF, 60-89 mL/min (n=109)</th>
<th>GF ≥90 mL/min (n=77)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean (SD), y</td>
<td>55 (13)</td>
<td>58.59 (12.1)</td>
<td>49.92 (12.4)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Men</td>
<td>108 (58.1)</td>
<td>64 (58.7)</td>
<td>33 (57.1)</td>
<td>NS</td>
</tr>
<tr>
<td>Diabetes</td>
<td>29 (15.6)</td>
<td>17 (15.6)</td>
<td>12 (15.6)</td>
<td>NS</td>
</tr>
<tr>
<td>Smoker</td>
<td>47 (25.5)</td>
<td>18 (16.6)</td>
<td>29 (37.7)</td>
<td>.005</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>64 (34.4)</td>
<td>42 (38.5)</td>
<td>22 (28.6)</td>
<td>NS</td>
</tr>
<tr>
<td>Ischemic heart disease</td>
<td>9 (4.8)</td>
<td>9 (8.3)</td>
<td>0</td>
<td>.01</td>
</tr>
<tr>
<td>Stroke</td>
<td>10 (5.4)</td>
<td>7 (6.4)</td>
<td>3 (3.9)</td>
<td>NS</td>
</tr>
<tr>
<td>LVH</td>
<td>51 (27.4)</td>
<td>30 (34.9)</td>
<td>13 (16.9)</td>
<td>.008</td>
</tr>
<tr>
<td>SAP, mmHg</td>
<td>152.6 (20.9)</td>
<td>154.5 (21.7)</td>
<td>149.9 (19.7)</td>
<td>NS</td>
</tr>
<tr>
<td>DAP, mmHg</td>
<td>89.1 (13.1)</td>
<td>89.3 (14.4)</td>
<td>88.8 (11)</td>
<td>NS</td>
</tr>
<tr>
<td>Weight, kg</td>
<td>82 (16.5)</td>
<td>81.9 (16.5)</td>
<td>82.2 (16.7)</td>
<td>NS</td>
</tr>
<tr>
<td>Height, m</td>
<td>1.65 (0.1)</td>
<td>1.64 (0.1)</td>
<td>1.65 (0.1)</td>
<td>NS</td>
</tr>
<tr>
<td>Glucose, mg/dL</td>
<td>111.2 (20)</td>
<td>112.1 (27.4)</td>
<td>110 (33.4)</td>
<td>NS</td>
</tr>
<tr>
<td>Creatinine, mg/dL</td>
<td>0.89 (0.2)</td>
<td>0.98 (0.2)</td>
<td>0.77 (0.1)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>MAU in 24 h, mg</td>
<td>61.4 (199.9)</td>
<td>78.9 (245.7)</td>
<td>39.17 (115.1)</td>
<td>NS</td>
</tr>
<tr>
<td>Aldosterone, ng/dL</td>
<td>18.1 (14.4)</td>
<td>20.1 (16.3)</td>
<td>15.3 (10.5)</td>
<td>.025</td>
</tr>
<tr>
<td>PRA, ng/mL/h</td>
<td>2.9 (5.4)</td>
<td>2.9 (5.2)</td>
<td>2.8 (5.7)</td>
<td>NS</td>
</tr>
<tr>
<td>GFR, mL/min</td>
<td>87.1 (16)</td>
<td>75.5 (8.3)</td>
<td>103.5 (11.8)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>NT-proBNP, pg/mL</td>
<td>130.7 (184.6)</td>
<td>160.6 (212)</td>
<td>92.6 (133.3)</td>
<td>.025</td>
</tr>
</tbody>
</table>

DAP indicates diastolic arterial pressure; GFR, glomerular filtration rate; LVH, left ventricular hypertrophy; MAU, microalbuminuria; NT-proBNP, n-terminal probrain natriuretic peptide; PRA, plasma renin activity; SAP, systolic arterial pressure

The data express the mean (standard deviation) or number (%).
In addition, the results from several clinical trials support the hypothesis that aldosterone can independently produce renal and cardiac damage in patients without hyperaldosteronism. It is known that in advanced stages of renal failure, aldosterone values usually increase secondary to activation of the renin-angiotensin-aldosterone system, and this can contribute to greater organ damage and create a vicious circle. Nonetheless, in hypertensive patients with preserved renal function, there are no clinical reports that specifically investigate the possible relationship between aldosterone and renal function.

It is mainly in experimental animal studies where the damage caused by aldosterone has been analyzed at different levels of the nephron, such as the mesangium, basement membrane, and renal tubule. These studies indicate an important pathologic role of the hormone in renal function deterioration. It seems clear that aldosterone is an important mediator of collagen turnover, stimulating the expression of various profibrotic molecules and inhibiting other antifibrotic molecules, thereby assuming a decisive role in the development of renal and cardiac fibrosis. In this last aspect, the present study brings to light a possible deleterious effect of aldosterone on the heart, as manifested by a higher prevalence of ischemic heart disease in patients with higher aldosterone concentrations, which has been described previously in patients with hyperaldosteronism and a significant correlation with the left ventricular mass adjusted by body surface area (r=0.167; P<.05).

Our findings underscore the interesting association between plasma aldosterone concentration and deteriorated renal function in the initial phases of patients with hypertension. Studies in this field are needed to analyze whether more effective and intensive blockade of aldosterone secretion could be effective in preventing renal function deterioration in these patients.

REFERENCES